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(54) Title: NOVEL MOLECULES OF THE TANGO-77 RELATED PROTEIN FAMILY AND USES THEREOF

(57) Abstract

Novel Tango-77 polypeptides, proteins, and nucleic acid molecules are disclosed. In addition to isolated, full-length Tango-77 proteins, the invention further provides isolated Tango-77 fusion proteins, antigenic peptides and anti-Tango-77 antibodies. The invention also provides Tango-77 nucleic acid molecules, recombinant expression vectors containing a nucleic acid molecule of the invention, host cells into which the expression vectors have been introduced and non-human transgenic animals in which a Tango-77 gene has been introduced or disrupted. Diagnostic, screening and therapeutic methods utilizing compositions of the invention are also provided.

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NOVEL MOLECULES OF THE TANGO-77 RELATED PROTEIN  
FAMILY AND USES THEREOF

Background of the Invention

The polypeptide cytokine interleukin-1 (IL-1) is a critical mediator of inflammatory and overall immune response. To date, three members of the IL-1 family, IL-1 $\alpha$ , IL-1 $\beta$  and IL-1ra (Interleukin-1 receptor antagonist) have been isolated and cloned. IL-1 $\alpha$  and IL-1 $\beta$  are proinflammatory cytokines which elicit biological responses, whereas IL-1ra is an antagonist of IL-1 $\alpha$  and IL-1 $\beta$  activity. Two distinct cell-surface receptors have been identified for these ligands, the type I IL-1 receptor (IL-1RtI) and type II IL-1 receptor (IL-1RtII). Recent results suggest that the IL-1RtI is the receptor responsible for transducing a signal and producing biological effects.

As mentioned above, IL-1 is a key mediator of the host inflammatory response. While inflammation is an important homeostatic mechanism, aberrant inflammation has the potential for inducing damage to the host. Elevated IL-1 levels are known to be associated with a number of diseases particularly autoimmune diseases and inflammatory disorders.

Since IL-1ra is a naturally occurring inhibitor of IL-1, IL-1ra can be used to limit the aberrant and potentially deleterious effects of IL-1. In experimental animals, pretreatment with IL-1ra has been shown to prevent death resulting from lipopolysaccharide-induced sepsis. The relative absence of IL-1ra has also been suggested to play a role in human inflammatory bowel disease.

Summary of the Invention

The present invention is based, at least in part, on the discovery of a gene encoding Tango-77, a secreted

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protein that is predicted to be a member of the cytokine superfamily. The Tango-77 cDNA described below (SEQ ID NO:1) has three possible open reading frames. The first potential open reading frame encompasses 534 nucleotides  
5 extending from nucleotide 356 to nucleotide 889 of SEQ ID NO:1 (SEQ ID NO:3) and encodes a 178 amino acid protein (SEQ ID NO:2). This protein may include a predicted signal sequence of about 63 amino acids (from about amino acid 1 to about amino acid 63 of SEQ ID NO:2 (SEQ ID  
10 NO:4) and a predicted mature protein of about 115 amino acids (from about amino acid 64 to amino acid 178 of SEQ ID NO:2 (SEQ ID NO:5)).

The second potential open reading frame encompasses 498 nucleotides extending from nucleotide 389  
15 to nucleotide 889 of SEQ ID NO:1 (SEQ ID NO:6) and encodes a 167 amino acid protein (SEQ ID NO:7). This protein may include a predicted signal sequence of about 52 amino acids (from about amino acid 1 to about amino acid 52 of SEQ ID NO:7 (SEQ ID NO:8)) and a predicted  
20 mature protein of about 115 amino acids (from about amino acid 52 to amino acid 167 of SEQ ID NO:7 (SEQ ID NO:9)).

The third potential open reading frame encompasses 408 nucleotides extending from nucleotide 481 to nucleotide 889 of SEQ ID NO:1 (SEQ ID NO:10) and encodes  
25 a 136 amino acid protein (SEQ ID NO:11). This protein includes a predicted signal sequence of about 21 amino acids (from about amino acid 1 to about amino acid 21 of SEQ ID NO:11 (SEQ ID NO:12)) and a predicted mature protein of about 115 amino acids (from about amino acid  
30 22 to amino acid 136 of SEQ ID NO:11 (SEQ ID NO:13)).

As used herein, the terms "Tango-77", "Tango-77 protein", "Tango-77 polypeptide" and the like, can refer and polypeptide produced by the cDNA of SEQ ID NO:1 including any and all of the Tango-77 gene products  
35 described above.



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Tango-77 is expected to inhibit inflammation and play a functional role similar to that of secreted IL-1ra. For example, it is expected that Tango-77 may bind to the IL-1 receptor, thus blocking receptor activation by inhibiting the binding of IL-1 $\alpha$  and IL-1 $\beta$  to the receptor. Alternatively, Tango-77 may inhibit inflammation through another pathway, for example, by binding to a novel receptor. Accordingly, Tango-77 may be useful as a modulating agent in regulating a variety of cellular processes including acute and chronic inflammation, e.g., asthma, chronic myelogenous leukemia, rheumatoid arthritis, psoriasis and inflammatory bowel disease.

In one aspect, the invention provides isolated nucleic acid molecules encoding Tango-77 or biologically active portions thereof, as well as nucleic acid fragments suitable as primers or hybridization probes for the detection of Tango-77.

The invention encompasses methods of diagnosing and treating patients who are suffering from a disorder associated with an abnormal level (undesirably high or undesirably low) of inflammation, abnormal activity of the IL-1 receptor complex, or abnormal activity of IL-1, by administering a compound that modulates the expression of Tango-77 (at the DNA, mRNA or protein level, e.g., by altering mRNA splicing) or by altering the activity of Tango-77. Examples of such compounds include small molecules, antisense nucleic acid molecules, ribozymes, and polypeptides.

The invention features a nucleic acid molecule which is at least 45% (e.g., 55%, 65%, 75%, 85%, 95%, or 98%) identical to the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the nucleotide sequence of the cDNA insert of the plasmid

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deposited with ATCC as Accession Number (the "cDNA of ATCC 98807"), or a complement thereof.

The invention features a nucleic acid molecule which includes a fragment of at least 100 (e.g., 250, 325, 350, 375, 400, 425, 450, 500, 550, 600, 650, 700, 800, 900, or 989) nucleotides of the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the nucleotide sequence of the cDNA ATCC 98807, or a complement thereof.

10 The invention also features a nucleic acid molecule which includes a nucleotide sequence encoding a protein having an amino acid sequence that is at least 45% (55%, 65%, 75%, 85%, 95%, or 98%) identical to the amino acid sequence of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, or the amino acid sequence encoded by the cDNA of ATCC 98807.

In a preferred embodiment, a Tango-77 nucleic acid molecule has the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the 20 nucleotide sequence of the cDNA of ATCC 98807.

Also within the invention is a nucleic acid molecule which encodes a fragment of a polypeptide having the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, wherein the fragment 25 includes at least 15 (e.g., 25, 30, 50, 100, 150, or 178) contiguous amino acids of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or the polypeptide 30 encoded by the cDNA of ATCC Accession Number 98807.

The invention includes a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, 35 SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or

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an amino acid sequence encoded by the cDNA of ATCC Accession Number 98807, wherein the nucleic acid molecule hybridizes to a nucleic acid molecule comprising SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or a  
5 complement thereof under stringent conditions.

Also within the invention are: an isolated Tango-77 protein having an amino acid sequence that is at least about 45%, preferably 65%, 75%, 85%, 95%, or 98% identical to the amino acid sequence of SEQ ID NO:5, SEQ  
10 ID NO:9 or SEQ ID NO:13 (mature human Tango-77), or the amino acid sequence of SEQ ID NO:2, SEQ ID NO:7 or SEQ ID NO:11 (immature human Tango-77).

Also within the invention are: an isolated Tango-77 protein which is encoded by a nucleic acid  
15 molecule having a nucleotide sequence that is at least about 65%, preferably 75%, 85%, or 95% identical to SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the cDNA of ATCC 98807; and an isolated Tango-77 protein which is encoded by a nucleic acid molecule having a nucleotide sequence  
20 which hybridizes under stringent hybridization conditions to a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the non-coding strand of the cDNA of ATCC 98807, or the complement thereof.

25 Also within the invention is a polypeptide which is a naturally occurring allelic variant of a polypeptide that includes the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an  
30 amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, wherein the polypeptide is encoded by a nucleic acid molecule which hybridizes to a nucleic acid molecule comprising SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID

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NO:10 or the complement thereof under stringent conditions.

Another embodiment of the invention features Tango-77 nucleic acid molecules which specifically detect  
5 Tango-77 nucleic acid molecules relative to nucleic acid molecules encoding other members of the cytokine superfamily. For example, in one embodiment, a Tango-77 nucleic acid molecule hybridizes under stringent conditions to a nucleic acid molecule comprising the  
10 nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or a complement thereof. In another embodiment, the Tango-77 nucleic acid molecule is at least 300 (325, 350, 375, 400, 425, 450, 500, 550, 600, 650, 700, 800, 900, or 989)  
15 nucleotides in length and hybridizes under stringent conditions to a nucleic acid molecule comprising the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or a complement thereof. In yet another embodiment, the  
20 invention provides an isolated nucleic acid molecule which is antisense to the coding strand of a Tango-77 nucleic acid.

Another aspect of the invention provides a vector, e.g., a recombinant expression vector, comprising a  
25 Tango-77 nucleic acid molecule of the invention. In another embodiment, the invention provides a host cell containing such a vector. The invention also provides a method for producing Tango-77 protein by culturing, in a suitable medium, a host cell of the invention containing  
30 a recombinant expression vector such that a Tango-77 protein is produced.

Another aspect of this invention features isolated or recombinant Tango-77 proteins and polypeptides. Preferred Tango-77 proteins and polypeptides possess at  
35 least one biological activity possessed by naturally

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occurring human Tango-77, e.g., (i) the ability to interact with proteins in the Tango-77 signalling pathway (ii) the ability to interact with a Tango-77 ligand or receptor; or (iii) the ability to interact with an intracellular target protein, (iv) the ability to interact with a protein involved in inflammation and (v) the ability to bind the IL-1 receptor. Other activities include the induction and suppression of polypeptide interleukins, cytokines and growth factors.

10       The Tango-77 proteins of the present invention, or biologically active portions thereof, can be operably linked to a non-Tango-77 polypeptide (e.g., heterologous amino acid sequences) to form Tango-77 fusion proteins. The invention further features antibodies that  
15 specifically bind Tango-77 proteins, such as monoclonal or polyclonal antibodies. In addition, the Tango-77 proteins or biologically active portions thereof can be incorporated into pharmaceutical compositions, which optionally include pharmaceutically acceptable carriers.

20       In another aspect, the present invention provides a method for detecting the presence of Tango-77 activity or expression in a biological sample by contacting the biological sample with an agent capable of detecting an indicator of Tango-77 activity or expression such that  
25 the presence of Tango-77 activity or expression is detected in the biological sample.

In another aspect, the invention provides a method for modulating Tango-77 activity comprising contacting a cell with an agent that modulates (inhibits or  
30 stimulates)

Tango-77 activity or expression such that Tango-77 activity or expression in the cell is modulated. In one embodiment, the agent is an antibody that specifically binds to Tango-77 protein. In another embodiment, the

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agent modulates expression of Tango-77 by modulating transcription of a Tango-77 gene, splicing of a Tango-77 mRNA, or translation of a Tango-77 mRNA. In yet another embodiment, the agent is a nucleic acid molecule having a nucleotide sequence that is antisense to the coding strand of the Tango-77 mRNA or the Tango-77 gene.

In one embodiment, the methods of the present invention are used to treat a subject having a disorder characterized by aberrant Tango-77 protein activity or nucleic acid expression by administering an agent which is a Tango-77 modulator to the subject. In one embodiment, the Tango-77 modulator is a Tango-77 protein. In another embodiment, the Tango-77 modulator is a Tango-77 nucleic acid molecule. In other embodiments, the Tango-77 modulator is a peptide, peptidomimetic, or other small molecule. In a preferred embodiment, the disorder characterized by aberrant Tango-77 protein or nucleic acid expression can include chronic and acute inflammation.

The present invention also provides a diagnostic assay for identifying the presence or absence of a genetic lesion or mutation characterized by at least one of: (i) aberrant modification or mutation of a gene encoding a Tango-77 protein; (ii) mis-regulation of a gene encoding a Tango-77 protein; and (iii) aberrant post-translational modification of a Tango-77 protein, wherein a wild-type form of the gene encodes a protein with a Tango-77 activity.

In another aspect, the invention provides a method for identifying a compound that binds to or modulates the activity of a Tango-77 protein. In general, such methods entail measuring a biological activity of a Tango-77 protein in the presence and absence of a test compound and identifying those

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compounds which alter the activity of the Tango-77 protein.

The invention also features methods for identifying a compound which modulates the expression of Tango-77 by measuring the expression of Tango-77 in the presence and absence of a compound.

Other features and advantages of the invention will be apparent from the following detailed description and claims.

#### Brief Description of the Drawings

Figure 1 depicts the cDNA sequence (SEQ ID NO:1) of Tango-77. The Tango-77 cDNA has three possible open reading frames which encode the amino acid sequence (SEQ ID NO:2, SEQ ID NO:7 and SEQ ID NO:11) of human Tango-77. The three potential open reading frames of SEQ ID NO:1 extend from: (1) nucleotide 356 to nucleotide 889 (SEQ ID NO:3); (2) nucleotide 389 to nucleotide 889 (SEQ ID NO:6); and (3) nucleotide 481 to nucleotide 889 (SEQ ID NO:10).

Figure 2 depicts an alignment of an amino acid sequence of Tango-77 (T77; SEQ ID NO:2) with IL-1RA (SEQ ID NO:14), and IL-1 $\beta$  (SEQ ID NO:15).

Figure 3 depicts the genomic sequence of BAC1 (SEQ ID NO:16).

Figure 4 depicts the genomic sequence of BAC2 (SEQ ID NO:17).

Figure 5 depicts an amino acid sequence of an alternatively spliced form of Tango-77 (SEQ ID NO:2) as predicted by Procrustes (T77-procrustes; SEQ ID NO:18).

Figure 6 depicts an alignment of an amino acid sequence of an alternatively spliced form of Tango-77 (T77-procrustes; SEQ ID NO:18) with Tango-77 (SEQ ID NO:2).

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Figure 7 depicts an alignment of an amino acid sequence of an alternatively spliced form of Tango-77 (T77-procrustes; SEQ ID NO:18) with IL-1ra (SEQ ID NO:14), and IL-1 $\beta$  (SEQ ID NO:15).

5

#### Detailed Description of the Invention

The present invention is based on the discovery of a cDNA molecule encoding human Tango-77, a member of the cytokine superfamily. The cDNA molecule encoding human Tango-77 has three possible open reading frames. The  
10 three possible nucleotide open reading frames for human Tango-77 protein are shown in Figure 1 (SEQ ID NO:3, SEQ ID NO:6 and SEQ ID NO:10). The predicted amino acid sequence for the three possible Tango-77 immature proteins are also shown in  
15 Figure 1 (SEQ ID NO:2, SEQ ID NO:7 or SEQ ID NO:11) and three possible mature proteins are also shown in Figure 1 (SEQ ID NO:5, SEQ ID NO:9 and SEQ ID NO:13).

The Tango-77 cDNA of Figure 1 (SEQ ID NO:1), which is approximately 989 nucleotides long including  
20 untranslated regions, encodes a protein amino acid having a molecular weight of approximately 19 kDa, 18 kDa, or 14.9 kDa (excluding post-translational modifications) and the possible mature form of the protein has a molecular weight of 13 kDa. A plasmid containing a cDNA encoding  
25 human Tango-77 (with the cDNA insert name of Of fthx077) was deposited with American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, Virginia 20110-2209 on July 2, 1998 and assigned Accession Number 98807. This deposit will be maintained under the terms  
30 of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. This deposit was made merely as a convenience for those of skill in the art and is not an



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admission that a deposit is required under 35 U.S.C.  
§112.

Human Tango-77 is one member of a family of molecules (the "Tango-77 family") having certain  
5 conserved structural and functional features. The term "family," when referring to the protein and nucleic acid molecules of the invention, is intended to mean two or more proteins or nucleic acid molecules having a common structural domain and having sufficient amino acid or  
10 nucleotide sequence identity as defined herein. Such family members can be naturally occurring and can be from either the same or different species. For example, a family can contain a first protein of human origin and a  
15 second, distinct protein of human origin and a murine homologue of that protein. Members of a family may also have common functional characteristics.

As used interchangeably herein a "Tango-77 activity", "biological activity of Tango-77" or  
20 "functional activity of Tango-77", refers to an activity exerted by a Tango-77 protein, polypeptide or nucleic acid molecule on a Tango-77 responsive cell as determined in vivo, or in vitro, according to standard techniques. A Tango-77 activity can be a direct activity, such as an  
25 association with a second protein, or an indirect activity, such as a cellular signaling activity mediated by interaction of the Tango-77 protein with a second protein. In a preferred embodiment, a Tango-77 activity includes at least one or more of the following  
30 activities: (i) the ability to interact with proteins in the Tango-77 signalling pathway (ii) the ability to interact with a Tango-77 ligand or receptor; or (iii) the ability to interact with an intracellular target protein, (iv) the ability to interact with a protein involved in

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inflammation, and (v) the ability to bind the IL-1 receptor.

Accordingly, another embodiment of the invention features isolated Tango-77 proteins and polypeptides  
5 having a Tango-77 activity.

Yet another embodiment of the invention features Tango-77 molecules which contain a signal sequence. Generally, a signal sequence (or signal peptide) is a peptide containing about 21 to 63 amino acids which  
10 occurs at the extreme N-terminal end of a secretory protein. The native Tango-77 signal sequence (SEQ ID NO:4, SEQ ID NO:8, or SEQ ID NO:12) can be removed and replaced with a signal sequence from another protein. In certain host cells (e.g., mammalian host cells),  
15 expression and/or secretion of Tango-77 can be increased through use of a heterologous signal sequence. For example, the gp67 secretory sequence of the baculovirus envelope protein can be used as a heterologous signal sequence. Alternatively, the native Tango-77 signal  
20 sequence can itself be used as a heterologous signal sequence in expression systems, e.g., to facilitate the secretion of a protein of interest.

Various aspects of the invention are described in further detail in the following subsections.

25 I. Isolated Nucleic Acid Molecules

One aspect of the invention pertains to isolated nucleic acid molecules that encode Tango-77 proteins or biologically active portions thereof, as well as nucleic acid molecules sufficient for use as hybridization probes  
30 to identify Tango-77-encoding nucleic acids (e.g., Tango-77 mRNA) and fragments for use as PCR primers for the amplification or mutation of Tango-77 nucleic acid molecules. As used herein, the term "nucleic acid molecule" is intended to include DNA molecules (e.g.,

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cDNA or genomic DNA) and RNA molecules (e.g., mRNA) and analogs of the DNA or RNA generated using nucleotide analogs. The nucleic acid molecule can be single-stranded or double-stranded, but preferably is double-stranded DNA.

An "isolated" nucleic acid molecule is one which is separated from other nucleic acid molecules which are present in the natural source of the nucleic acid. Preferably, an "isolated" nucleic acid is free of sequences (preferably protein encoding sequences) which naturally flank the nucleic acid (i.e., sequences located at the 5' and 3' ends of the nucleic acid) in the genomic DNA of the organism from which the nucleic acid is derived. For example, in various embodiments, the isolated Tango-77 nucleic acid molecule can contain less than about 5 kb, 4 kb, 3 kb, 2 kb, 1 kb, 0.5 kb or 0.1 kb of nucleotide sequences which naturally flank the nucleic acid molecule in genomic DNA of the cell from which the nucleic acid is derived. Moreover, an "isolated" nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material, or culture medium when produced by recombinant techniques, or substantially free of chemical precursors or other chemicals when chemically synthesized.

A nucleic acid molecule of the present invention, e.g., a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or a complement of any of these nucleotide sequences, can be isolated using standard molecular biology techniques and the sequence information provided herein. Using all or a portion of the nucleic acid sequences of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or the complement thereof as a hybridization probe, Tango-77 nucleic acid molecules can be isolated using standard

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hybridization and cloning techniques (e.g., as described in Sambrook et al., eds., *Molecular Cloning: A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989).

A nucleic acid of the invention can be amplified using cDNA, mRNA or genomic DNA as a template and appropriate oligonucleotide primers according to standard PCR amplification techniques. The nucleic acid so  
10 amplified can be cloned into an appropriate vector and characterized by DNA sequence analysis. Furthermore, oligonucleotides corresponding to Tango-77 nucleotide sequences can be prepared by standard synthetic techniques, e.g., using an automated DNA synthesizer.

15 In another preferred embodiment, an isolated nucleic acid molecule of the invention comprises a nucleic acid molecule which is a complement of the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 the cDNA of ATCC 98807, or a  
20 portion thereof. A nucleic acid molecule which is complementary to a given nucleotide sequence is one which is sufficiently complementary to the given nucleotide sequence that it can hybridize to the given nucleotide sequence thereby forming a stable duplex.

25 Moreover, the nucleic acid molecule of the invention can comprise only a portion of a nucleic acid sequence encoding Tango-77, for example, a fragment which can be used as a probe or primer or a fragment encoding a biologically active portion of Tango-77. The nucleotide  
30 sequence determined from the cloning of the human Tango-77 gene allows for the generation of probes and primers designed for use in identifying and/or cloning Tango-77 homologues in other cell types, e.g., from other tissues, as well as Tango-77 homologues from other  
35 mammals. The probe/primer typically comprises

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substantially purified oligonucleotide. The oligonucleotide typically comprises a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12, preferably about 25, more preferably about 50, 75, 100, 125, 150, 175, 200, 250, 300, 350 or 400 consecutive nucleotides of the sense or anti-sense sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807. Alternatively, the oligonucleotide can typically comprise a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12, preferably about 25, more preferably about 50, 75, 100, 125, 150, 175, 200, 250, 300, 350 or 400 consecutive nucleotides of the sense or anti-sense sequence of a naturally occurring mutant of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807.

Probes based on the human Tango-77 nucleotide sequence can be used to detect transcripts or genomic sequences encoding the same or identical proteins. The probe comprises a label group attached thereto, e.g., a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor. Such probes can be used as a part of a diagnostic test kit for identifying cells or tissues which mis-express a Tango-77 protein, such as by measuring a level of a Tango-77-encoding nucleic acid in a sample of cells from a subject, e.g., detecting Tango-77 mRNA levels or determining whether a genomic Tango-77 gene has been mutated or deleted.

A nucleic acid fragment encoding a "biologically active portion of Tango-77" can be prepared by isolating a portion of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the nucleotide sequence of the cDNA of ATCC 98807 which encodes a polypeptide having a Tango-77 biological activity, expressing the encoded portion of Tango-77 protein (e.g., by recombinant expression in

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vitro) and assessing the activity of the encoded portion of Tango-77.

The invention further encompasses nucleic acid molecules that differ from the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807 due to degeneracy of the genetic code and thus encode the same Tango-77 protein as that encoded by the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807.

In addition to the human Tango-77 nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807, it will be appreciated by those skilled in the art that DNA sequence polymorphisms that lead to changes in the amino acid sequences of Tango-77 may exist within a population (e.g., the human population). Such genetic polymorphism in the Tango-77 gene may exist among individuals within a population due to natural allelic variation. An allele is one of a group of genes which occur alternatively at a given genetic locus. As used herein, the term "allelic variant" refers to a nucleotide sequence which occurs at a Tango-77 locus or to a polypeptide encoded by the nucleotide sequence. As used herein, the terms "gene" and "recombinant gene" refer to nucleic acid molecules comprising an open reading frame encoding a Tango-77 protein, preferably a mammalian Tango-77 protein. Such natural allelic variations can typically result in 1-5% variance in the nucleotide sequence of the Tango-77 gene. Alternative alleles can be identified by sequencing the gene of interest in a number of different individuals. This can be readily carried out by using hybridization probes to identify the same genetic locus in a variety of individuals. Any and all such nucleotide variations and resulting amino acid polymorphisms or variations in

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Tango-77 that are the result of natural allelic variation and that do not alter the functional activity of Tango-77 are intended to be within the scope of the invention.

Moreover, nucleic acid molecules encoding Tango-77  
5 proteins from other species (Tango-77 homologues), which have a nucleotide sequence which differs from that of a human Tango-77, are intended to be within the scope of the invention. Nucleic acid molecules corresponding to natural allelic variants and homologues of the Tango-77  
10 cDNA of the invention can be isolated based on their identity to the human Tango-77 nucleic acids disclosed herein using the human cDNAs, or a portion thereof, as a hybridization probe according to standard hybridization techniques under stringent hybridization conditions.

15 Accordingly, in another embodiment, an isolated nucleic acid molecule of the invention is at least 300 (325, 350, 375, 400, 425, 450, 500, 550, 600, 650, 700, 800, or 989) nucleotides in length and hybridizes under stringent conditions to the nucleic acid molecule  
20 comprising the nucleotide sequence, preferably the coding sequence, of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807.

As used herein, the term "hybridizes under stringent conditions" is intended to describe conditions  
25 for hybridization and washing under which nucleotide sequences at least 60% (65%, 70%, preferably 75%) identical to each other typically remain hybridized to each other. Such stringent conditions are known to those skilled in the art and can be found in *Current Protocols*  
30 *in Molecular Biology*, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6. A preferred, non-limiting example of stringent hybridization conditions are hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at  
35 50-65°C. Preferably, an isolated nucleic acid molecule

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of the invention that hybridizes under stringent conditions to the sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or the complement thereof, corresponds to a naturally-occurring  
5 nucleic acid molecule. As used herein, a "naturally-occurring" nucleic acid molecule refers to an RNA or DNA molecule having a nucleotide sequence that occurs in nature (e.g., encodes a natural protein).

In addition to naturally-occurring allelic  
10 variants of the Tango-77 sequence that may exist in the population, the skilled artisan will further appreciate that changes can be introduced by mutation into the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the cDNA of ATCC 98807, thereby  
15 leading to changes in the amino acid sequence of the encoded Tango-77 protein, without altering the biological activity of the Tango-77 protein. Amino acid residues that are not conserved or only semiconserved among Tango-77 of various species may be non-essential for activity  
20 and thus would likely be targets for alteration. Alternatively, one can make nucleotide substitutions leading to amino acid substitutions at "non-essential" amino acid residues. A "non-essential" amino acid residue is a residue that can be altered from the wild-  
25 type sequence of Tango-77 (e.g., the sequence of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11 or SEQ ID NO:13) without altering the biological activity, whereas an "essential" amino acid residue is required for biological activity. For example, amino  
30 acid residues that are conserved among the Tango-77 proteins of various species may be essential for activity and thus would not likely be targets for alteration, unless one wishes to reduce or alter Tango-77 activity.

Accordingly, another aspect of the invention  
35 pertains to nucleic acid molecules encoding Tango-77



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proteins that contain changes in amino acid residues that are not essential for activity. Such Tango-77 proteins differ in amino acid sequence from SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 yet retain biological activity. In one embodiment, the isolated nucleic acid molecule includes a nucleotide sequence encoding a protein that includes an amino acid sequence that is at least about 45% identical, 65%, 75%, 85%, 95%, or 98% identical to the amino acid sequence of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13.

An isolated nucleic acid molecule encoding a Tango-77 protein having a sequence which differs from that of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 can be created by introducing one or more nucleotide substitutions, additions or deletions into the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807 such that one or more amino acid substitutions, additions or deletions are introduced into the encoded protein. Mutations can be introduced by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted non-essential amino acid residues. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (e.g., alanine,

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valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine).

5 Thus, a predicted nonessential amino acid residue in Tango-77 is preferably replaced with another amino acid residue from the same side chain family. Alternatively, mutations can be introduced randomly along all or part of a Tango-77 coding sequence, such as by saturation  
10 mutagenesis, and the resultant mutants can be screened for Tango-77 biological activity to identify mutants that retain activity. Following mutagenesis, the encoded protein can be expressed recombinantly and the activity of the protein can be determined.

15 In a preferred embodiment, a mutant Tango-77 protein can be assayed for: (1) the ability to form protein:protein interactions with proteins in the Tango-77 signalling pathway; (2) the ability to bind a Tango-77 ligand or receptor; or (3) the ability to bind  
20 to an intracellular target protein or (4) the ability to interact with a protein involved in inflammation or (5) the ability to bind the IL-1 receptor. In yet another preferred embodiment, a mutant Tango-77 can be assayed for the ability to modulate inflammation, asthma,  
25 autoimmune diseases, and sepsis.

The present invention encompasses antisense nucleic acid molecules, i.e., molecules which are complementary to a sense nucleic acid encoding a protein, e.g., complementary to the coding strand of a double-  
30 stranded cDNA molecule or complementary to an mRNA sequence. Accordingly, an antisense nucleic acid can hydrogen bond to a sense nucleic acid. The antisense nucleic acid can be complementary to an entire Tango-77 coding strand, or to only a portion thereof, e.g., all or  
35 part of the protein coding region (or open reading

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frame). An antisense nucleic acid molecule can be antisense to a noncoding region of the coding strand of a nucleotide sequence encoding Tango-77. The noncoding regions ("5' and 3' untranslated regions") are the 5' and 3' sequences which flank the coding region and are not translated into amino acids.

Given the coding strand sequences encoding Tango-77 disclosed herein (e.g., SEQ ID NO:3, SEQ ID NO:5, or SEQ ID NO:8), antisense nucleic acids of the invention can be designed according to the rules of Watson and Crick base pairing. The antisense nucleic acid molecule can be complementary to the entire coding region of Tango-77 mRNA, but more preferably is an oligonucleotide which is antisense to only a portion of the coding or noncoding region of Tango-77 mRNA. For example, the antisense oligonucleotide can be complementary to the region surrounding the translation start site of Tango-77 mRNA, e.g., an oligonucleotide having the sequence 5'-TGCAACTTTTACAGGAAACAC-3' (SEQ ID NO:19) or 5'-CCTCACTTTTACCCGAGACTC-3' (SEQ ID NO:20) or 5'-GACGGGTGGTACTTAAACAA-3' (SEQ ID NO:21). An antisense oligonucleotide can be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45 or 50 nucleotides in length. An antisense nucleic acid of the invention can be constructed using chemical synthesis and enzymatic ligation reactions using procedures known in the art. For example, an antisense nucleic acid (e.g., an antisense oligonucleotide) can be chemically synthesized using naturally occurring nucleotides or variously modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids, e.g., phosphorothioate derivatives and acridine substituted nucleotides can be used. Examples of modified nucleotides which can be used to

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generate the antisense nucleic acid include 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxymethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil (acp3)w, and 2,6-diaminopurine. Alternatively, the antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been subcloned in an antisense orientation (i.e., RNA transcribed from the inserted nucleic acid will be of an antisense orientation to a target nucleic acid of interest, described further in the following subsection).

The antisense nucleic acid molecules of the invention are typically administered to a subject or generated *in situ* such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding a Tango-77 protein to thereby inhibit expression of the protein, e.g., by inhibiting transcription and/or translation. The hybridization can be by conventional nucleotide complementarity to form a stable duplex, or, for example, in the case of an antisense nucleic acid molecule which

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binds to DNA duplexes, through specific interactions in the major groove of the double helix. An example of a route of administration of antisense nucleic acid molecules of the invention includes direct injection at a tissue site. Alternatively, antisense nucleic acid molecules can be modified to target selected cells and then administered systemically. For example, for systemic administration, antisense molecules can be modified such that they specifically bind to receptors or antigens expressed on a selected cell surface, e.g., by linking the antisense nucleic acid molecules to peptides or antibodies which bind to cell surface receptors or antigens. The antisense nucleic acid molecules can also be delivered to cells using the vectors described herein. To achieve sufficient intracellular concentrations of the antisense molecules, vector constructs in which the antisense nucleic acid molecule is placed under the control of a strong pol II or pol III promoter are preferred.

An antisense nucleic acid molecule of the invention can be an  $\alpha$ -anomeric nucleic acid molecule. An  $\alpha$ -anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual  $\beta$ -units, the strands run parallel to each other (Gaultier et al. (1987) *Nucleic Acids Res.* 15:6625-6641). The antisense nucleic acid molecule can also comprise a 2'-O-methylribonucleotide (Inoue et al. (1987) *Nucleic Acids Res.* 15:6131-6148) or a chimeric RNA-DNA analogue (Inoue et al. (1987) *FEBS Lett.* 215:327-330).

The invention also encompasses ribozymes. Ribozymes are catalytic RNA molecules with ribonuclease activity which are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Thus, ribozymes (e.g., hammerhead

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ribozymes (described in Haselhoff and Gerlach (1988) Nature 334:585-591)) can be used to catalytically cleave Tango-77 mRNA transcripts to thereby inhibit translation of Tango-77 mRNA. A ribozyme having specificity for a Tango-77-encoding nucleic acid can be designed based upon the nucleotide sequence of a Tango-77 cDNA disclosed herein (e.g., SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10). For example, a derivative of a *Tetrahymena* L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved in a Tango-77-encoding mRNA. See, e.g., Cech et al. U.S. Patent No. 4,987,071; and Cech et al. U.S. Patent No. 5,116,742. Alternatively, Tango-77 mRNA can be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See, e.g., Bartel and Szostak (1993) *Science* 261:1411-1418.

The invention also encompasses nucleic acid molecules which form triple helical structures. For example, Tango-77 gene expression can be inhibited by targeting nucleotide sequences complementary to the regulatory region of the Tango-77 (e.g., the Tango-77 promoter and/or enhancers) to form triple helical structures that prevent transcription of the Tango-77 gene in target cells. See generally, Helene (1991) *Anticancer Drug Des.* 6(6):569-84; Helene (1992) *Ann. N.Y. Acad. Sci.* 660:27-36; and Maher (1992) *Bioassays* 14(12):807-15.

In preferred embodiments, the nucleic acid molecules of the invention can be modified at the base moiety, sugar moiety or phosphate backbone to improve, e.g., the stability, hybridization, or solubility of the molecule. For example, the deoxyribose phosphate backbone of the nucleic acids can be modified to generate peptide nucleic acids (see Hyrup et al. (1996) *Bioorganic*

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& Medicinal Chemistry 4(1): 5-23). As used herein, the terms "peptide nucleic acids" or "PNAs" refer to nucleic acid mimics, e.g., DNA mimics, in which the deoxyribose phosphate backbone is replaced by a pseudopeptide backbone and only the four natural nucleobases are retained. The neutral backbone of PNAs has been shown to allow for specific hybridization to DNA and RNA under conditions of low ionic strength. The synthesis of PNA oligomers can be performed using standard solid phase peptide synthesis protocols as described in Hyrup et al. (1996) *supra*; Perry-O'Keefe et al. (1996) *Proc. Natl. Acad. Sci. USA* 93: 14670-675.

PNAs of Tango-77 can be used in therapeutic and diagnostic applications. For example, PNAs can be used as antisense or antigene agents for sequence-specific modulation of gene expression by, e.g., inducing transcription or translation arrest or inhibiting replication. PNAs of Tango-77 can also be used, e.g., in the analysis of single base pair mutations in a gene by, e.g., PNA directed PCR clamping; as artificial restriction enzymes when used in combination with other enzymes, e.g., S1 nucleases (Hyrup (1996) *supra*; or as probes or primers for DNA sequence and hybridization (Hyrup (1996) *supra*; Perry-O'Keefe et al. (1996) *Proc. Natl. Acad. Sci. USA* 93: 14670-675).

In another embodiment, PNAs of Tango-77 can be modified, e.g., to enhance their stability or cellular uptake, by attaching lipophilic or other helper groups to PNA, by the formation of PNA-DNA chimeras, or by the use of liposomes or other techniques of drug delivery known in the art. For example, PNA-DNA chimeras of Tango-77 can be generated which may combine the advantageous properties of PNA and DNA. Such chimeras allow DNA recognition enzymes, e.g., RNase H and DNA polymerases, to interact with the DNA portion while the PNA portion

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would provide high binding affinity and specificity. PNA-DNA chimeras can be linked using linkers of appropriate lengths selected in terms of base stacking, number of bonds between the nucleobases, and orientation (Hyrup (1996) *supra*). The synthesis of PNA-DNA chimeras can be performed as described in Hyrup (1996) *supra* and Finn et al. (1996) *Nucleic Acids Res.* 24(17):3357-63. For example, a DNA chain can be synthesized on a solid support using standard phosphoramidite coupling chemistry and modified nucleoside analogs. Compounds such as 5'-(4-methoxytrityl)amino-5'-deoxy-thymidine phosphoramidite can be used as a link between the PNA and the 5' end of DNA (Mag et al. (1989) *Nucleic Acid Res.* 17:5973-88). PNA monomers are then coupled in a stepwise manner to produce a chimeric molecule with a 5' PNA segment and a 3' DNA segment (Finn et al. (1996) *Nucleic Acids Res.* 24(17):3357-63). Alternatively, chimeric molecules can be synthesized with a 5' DNA segment and a 3' PNA segment (Peterser et al. (1975) *Bioorganic Med. Chem. Lett.* 5:1119-11124).

In other embodiments, the oligonucleotide may include other appended groups such as peptides (e.g., for targeting host cell receptors *in vivo*), or agents facilitating transport across the cell membrane (see, e.g., Letsinger et al. (1989) *Proc. Natl. Acad. Sci. USA* 86:6553-6556; Lemaitre et al. (1987) *Proc. Natl. Acad. Sci. USA* 84:648-652; PCT Publication No. W0 88/09810) or the blood-brain barrier (see, e.g., PCT Publication No. W0 89/10134). In addition, oligonucleotides can be modified with hybridization-triggered cleavage agents (see, e.g., Krol et al. (1988) *Bio/Techniques* 6:958-976) or intercalating agents (see, e.g., Zon (1988) *Pharm. Res.* 5:539-549). To this end, the oligonucleotide may be conjugated to another molecule, e.g., a peptide,



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hybridization triggered cross-linking agent, transport agent, hybridization-triggered cleavage agent, etc.

## II. Isolated Tango-77 Proteins and Anti-Tango-77 Antibodies

5 One aspect of the invention pertains to isolated Tango-77 proteins, and biologically active portions thereof, as well as polypeptide fragments suitable for use as immunogens to raise anti-Tango-77 antibodies. In one embodiment, native Tango-77 proteins can be isolated  
10 from cells or tissue sources by an appropriate purification scheme using standard protein purification techniques. In another embodiment, Tango-77 proteins are produced by recombinant DNA techniques. Alternative to recombinant expression, a Tango-77 protein or polypeptide  
15 can be synthesized chemically using standard peptide synthesis techniques.

An "isolated" or "purified" protein or biologically active portion thereof is substantially free of cellular material or other contaminating proteins from  
20 the cell or tissue source from which the Tango-77 protein is derived, or substantially free of chemical precursors or other chemicals when chemically synthesized. The language "substantially free of cellular material" includes preparations of Tango-77 protein in which the  
25 protein is separated from cellular components of the cells from which it is isolated or recombinantly produced. Thus, Tango-77 protein that is substantially free of cellular material includes preparations of Tango-77 protein having less than about 30%, 20%, 10%, or  
30 5% (by dry weight) of non-Tango-77 protein (also referred to herein as a "contaminating protein"). When the Tango-77 protein or biologically active portion thereof is recombinantly produced, it is also preferably substantially free of culture medium, i.e., culture

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medium represents less than about 20%, 10%, or 5% of the volume of the protein preparation. When Tango-77 protein is produced by chemical synthesis, it is preferably substantially free of chemical precursors or other chemicals, i.e., it is separated from chemical precursors or other chemicals which are involved in the synthesis of the protein. Accordingly such preparations of Tango-77 protein have less than about 30%, 20%, 10%, 5% (by dry weight) of chemical precursors or non-Tango-77 chemicals.

Biologically active portions of a Tango-77 protein include peptides comprising amino acid sequences sufficiently identical to or derived from the amino acid sequence of the Tango-77 protein (e.g., the amino acid sequence shown in SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13), which include fewer amino acids than the full length Tango-77 proteins, and exhibit at least one activity of a Tango-77 protein. Typically, biologically active portions comprise a domain or motif with at least one activity of the Tango-77 protein. A biologically active portion of a Tango-77 protein can be a polypeptide which is, for example, 10, 25, 50, 100 or more amino acids in length.

Moreover, other biologically active portions, in which other regions of the protein are deleted, can be prepared by recombinant techniques and evaluated for one or more of the functional activities of a native Tango-77 protein.

Preferred Tango-77 protein has the amino acid sequence shown of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13. Other useful Tango-77 proteins are substantially identical to SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 and retain the functional activity of the protein of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 yet differ in

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amino acid sequence due to natural allelic variation or mutagenesis. Accordingly, a useful Tango-77 protein is a protein which includes an amino acid sequence at least about 45%, preferably 55%, 65%, 75%, 85%, 95%, or 99% identical to the amino acid sequence of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 and retains the functional activity of the Tango-77 proteins of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13. In a preferred embodiment, the Tango-77 protein retains a functional activity of the Tango-77 protein of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13.

To determine the percent identity of two amino acid sequences or of two nucleic acids, the sequences are aligned for optimal comparison purposes (e.g., gaps can be introduced in the sequence of a first amino acid or nucleic acid sequence for optimal alignment with a second amino or nucleic acid sequence). The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position. The percent identity between the two sequences is a function of the number of identical positions shared by the sequences (i.e., % identity = # of identical positions/total # of positions, e.g., overlapping x 100). Preferably, the two sequences are the same length.

The determination of percent homology between two sequences can be accomplished using a mathematical algorithm. A preferred, non-limiting example of a mathematical algorithm utilized for the comparison of two sequences is the algorithm of Karlin and Altschul (1990)

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Proc. Natl. Acad. Sci. USA 87:2264-2268, modified as in Karlin and Altschul (1993) Proc. Natl. Acad. Sci. USA 90:5873-5877. Such an algorithm is incorporated into the NBLAST and XBLAST programs of Altschul, et al. (1990)

5 J. Mol. Biol. 215:403-410. BLAST nucleotide searches can be performed with the NBLAST program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to Tango-77 nucleic acid molecules of the invention. BLAST protein searches can be performed with the XBLAST

10 program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to Tango-77 protein molecules of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al. (1997) Nucleic Acids Res. 25:3389-3402.

15 When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) can be used. See <http://www.ncbi.nlm.nih.gov>. Another preferred, non-limiting example of a mathematical algorithm utilized for

20 the comparison of sequences is the algorithm of Myers and Miller, CABIOS (1989). Such an algorithm is incorporated into the ALIGN program (version 2.0) which is part of the GCG sequence alignment software package. When utilizing the ALIGN program for comparing amino acid sequences, a

25 PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4 can be used.

The percent identity between two sequences can be determined using techniques similar to those described above, with or without allowing gaps. In calculating

30 percent identity, only exact matches are counted.

The invention also provides Tango-77 chimeric or fusion proteins. As used herein, a Tango-77 "chimeric protein" or "fusion protein" comprises a Tango-77 polypeptide operably linked to a non-Tango-77

35 polypeptide. A "Tango-77 polypeptide" refers to a

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polypeptide having an amino acid sequence corresponding to Tango-77 polypeptides, whereas a "non-Tango-77 polypeptide" refers to a polypeptide having an amino acid sequence corresponding to a protein which is not

5 substantially identical to the Tango-77 protein, e.g., a protein which is different from the Tango-77 protein and which is derived from the same or a different organism. Within a Tango-77 fusion protein the Tango-77 polypeptide can correspond to all or a portion of a Tango-77 protein,

10 preferably at least one biologically active portion of a Tango-77 protein. Within the fusion protein, the term "operably linked" is intended to indicate that the Tango-77 polypeptide and the non-Tango-77 polypeptide are fused in-frame to each other. The non-Tango-77

15 polypeptide can be fused to the N-terminus or C-terminus of the Tango-77 polypeptide.

One useful fusion protein is a GST-Tango-77 fusion protein in which the Tango-77 sequences are fused to the C-terminus of the GST sequences. Such fusion proteins

20 can facilitate the purification of recombinant Tango-77.

In another embodiment, the fusion protein is a Tango-77 protein containing a heterologous signal sequence at its N-terminus. For example, the native Tango-77 signal sequence (i.e., about amino acids 1 to 63

25 of SEQ ID NO:2; SEQ ID NO:4; or about amino acids 1 to 52 of SEQ ID NO:7; SEQ ID NO:8; or about amino acids 1 to 21 of SEQ ID NO:11; SEQ ID NO:12) can be removed and replaced with a signal sequence from another protein. In certain host cells (e.g., mammalian host cells), expression

30 and/or secretion of Tango-77 can be increased through use of a heterologous signal sequence. For example, the gp67 secretory sequence of the baculovirus envelope protein can be used as a heterologous signal sequence (Ausubel et al., supra). Other examples of eukaryotic heterologous

35 signal sequences include the secretory sequences of

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melittin and human placental alkaline phosphatase (Stratagene; La Jolla, California). In yet another example, useful prokaryotic heterologous signal sequences include the phoA secretory signal (Sambrook et al.,  
5 supra) and the protein A secretory signal (Pharmacia Biotech; Piscataway, New Jersey).

In yet another embodiment, the fusion protein is an Tango-77-immunoglobulin fusion protein in which all or part of Tango-77 is fused to sequences derived from a  
10 member of the immunoglobulin protein family. The Tango-77-immunoglobulin fusion proteins of the invention can be incorporated into pharmaceutical compositions and administered to a subject to inhibit an interaction  
15 between a Tango-77 ligand and a Tango-77 receptor on the surface of a cell, to thereby suppress Tango-77-mediated signal transduction in vivo. The Tango-77-immunoglobulin fusion proteins can be used to affect the bioavailability of a Tango-77 cognate ligand. Inhibition of the Tango-77  
20 ligand/Tango-77 interaction may be useful therapeutically for both the treatment of inflammatory and autoimmune disorders. Moreover, the Tango-77-immunoglobulin fusion proteins of the invention can be used as immunogens to produce anti-Tango-77 antibodies in a subject, to purify  
25 Tango-77 ligands and in screening assays to identify molecules which inhibit the interaction of Tango-77 with a Tango-77 receptor.

Preferably, a Tango-77 chimeric or fusion protein of the invention is produced by standard recombinant DNA techniques. For example, DNA fragments coding for the  
30 different polypeptide sequences are ligated together in-frame in accordance with conventional techniques, for example by employing blunt-ended or stagger-ended termini for ligation, restriction enzyme digestion to provide for appropriate termini, filling-in of cohesive ends as  
35 appropriate, alkaline phosphatase treatment to avoid

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undesirable joining, and enzymatic ligation. In another embodiment, the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers. Alternatively, PCR amplification of gene fragments can be carried out using anchor primers which give rise to complementary overhangs between two consecutive gene fragments which can subsequently be annealed and reamplified to generate a chimeric gene sequence (see, e.g., *Current Protocols in Molecular Biology*, Ausubel et al. eds., John Wiley & Sons: 1992). Moreover, many expression vectors are commercially available that already encode a fusion moiety (e.g., a GST polypeptide). An Tango-77-encoding nucleic acid can be cloned into such an expression vector such that the fusion moiety is linked in-frame to the Tango-77 protein.

The present invention also pertains to variants of the Tango-77 proteins (i.e., proteins having a sequence which differs from that of the Tango-77 amino acid sequence). Such variants can function as either Tango-77 agonists (mimetics) or as Tango-77 antagonists. Variants of the Tango-77 protein can be generated by mutagenesis, e.g., discrete point mutation or truncation of the Tango-77 protein. An agonist of the Tango-77 protein can retain substantially the same, or a subset, of the biological activities of the naturally occurring form of the Tango-77 protein. An antagonist of the Tango-77 protein can inhibit one or more of the activities of the naturally occurring form of the Tango-77 protein by, for example, competitively binding to a downstream or upstream member of a cellular signaling cascade which includes the Tango-77 protein. Thus, specific biological effects can be elicited by treatment with a variant of limited function. Treatment of a subject with a variant having a subset of the biological activities of the naturally occurring form of the protein can have fewer

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side effects in a subject relative to treatment with the naturally occurring form of the Tango-77 proteins.

Variants of the Tango-77 protein which function as either Tango-77 agonists (mimetics) or as Tango-77  
5 antagonists can be identified by screening combinatorial libraries of mutants, e.g., truncation mutants, of the Tango-77 protein for Tango-77 protein agonist or antagonist activity. In one embodiment, a variegated library of Tango-77 variants is generated by  
10 combinatorial mutagenesis at the nucleic acid level and is encoded by a variegated gene library. A variegated library of Tango-77 variants can be produced by, for example, enzymatically ligating a mixture of synthetic oligonucleotides into gene sequences such that a  
15 degenerate set of potential Tango-77 sequences is expressible as individual polypeptides, or alternatively, as a set of larger fusion proteins (e.g., for phage display) containing the set of Tango-77 sequences therein. There are a variety of methods which can be  
20 used to produce libraries of potential Tango-77 variants from a degenerate oligonucleotide sequence. Chemical synthesis of a degenerate gene sequence can be performed in an automatic DNA synthesizer, and the synthetic gene then ligated into an appropriate expression vector. Use  
25 of a degenerate set of genes allows for the provision, in one mixture, of all of the sequences encoding the desired set of potential Tango-77 sequences. Methods for synthesizing degenerate oligonucleotides are known in the art (see, e.g., Narang (1983) *Tetrahedron* 39:3; Itakura  
30 et al. (1984) *Annu. Rev. Biochem.* 53:323; Itakura et al. (1984) *Science* 198:1056; Ike et al. (1983) *Nucleic Acid Res.* 11:477).

In addition, libraries of fragments of the Tango-77 protein coding sequence can be used to generate  
35 a variegated population of Tango-77 fragments for



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screening and subsequent selection of variants of a Tango-77 protein. In one embodiment, a library of coding sequence fragments can be generated by treating a double stranded PCR fragment of a Tango-77 coding sequence with  
5 a nuclease under conditions wherein nicking occurs only about once per molecule, denaturing the double stranded DNA, renaturing the DNA to form double stranded DNA which can include sense/antisense pairs from different nicked products, removing single stranded portions from reformed  
10 duplexes by treatment with S1 nuclease, and ligating the resulting fragment library into an expression vector. By this method, an expression library can be derived which encodes N-terminal and internal fragments of various sizes of the Tango-77 protein.

15 Several techniques are known in the art for screening gene products of combinatorial libraries made by point mutations or truncation, and for screening cDNA libraries for gene products having a selected property. Such techniques are adaptable for rapid screening of the  
20 gene libraries generated by the combinatorial mutagenesis of Tango-77 proteins. The most widely used techniques, which are amenable to high through-put analysis, for screening large gene libraries typically include cloning the gene library into replicable expression vectors,  
25 transforming appropriate cells with the resulting library of vectors, and expressing the combinatorial genes under conditions in which detection of a desired activity facilitates isolation of the vector encoding the gene whose product was detected. Recursive ensemble  
30 mutagenesis (REM), a technique which enhances the frequency of functional mutants in the libraries, can be used in combination with the screening assays to identify Tango-77 variants (Arkin and Yourvan (1992) *Proc. Natl. Acad. Sci. USA* 89:7811-7815; Delgrave et al. (1993)  
35 *Protein Engineering* 6(3):327-331).

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An isolated Tango-77 protein, or a portion or fragment thereof, can be used as an immunogen to generate antibodies that bind Tango-77 using standard techniques for polyclonal and monoclonal antibody preparation. The  
5 full-length Tango-77 protein can be used or, alternatively, the invention provides antigenic peptide fragments of Tango-77 for use as immunogens. The antigenic peptide of Tango-77 comprises at least 8 (preferably 10, 15, 20, or 30) amino acid residues of the  
10 amino acid sequence shown in SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11 or SEQ ID NO:13 and encompasses an epitope of Tango-77 such that an antibody raised against the peptide forms a specific immune complex with Tango-77.

15 A Tango-77 immunogen typically is used to prepare antibodies by immunizing a suitable subject (e.g., rabbit, goat, mouse or other mammal) with the immunogen. An appropriate immunogenic preparation can contain, for example, recombinantly expressed Tango-77 protein or a  
20 chemically synthesized Tango-77 polypeptide. The preparation can further include an adjuvant, such as Freund's complete or incomplete adjuvant, or similar immunostimulatory agent. Immunization of a suitable subject with an immunogenic Tango-77 preparation induces  
25 a polyclonal anti-Tango-77 antibody response.

Accordingly, another aspect of the invention pertains to anti-Tango-77 antibodies. The term "antibody" as used herein refers to immunoglobulin molecules and immunologically active portions of  
30 immunoglobulin molecules, i.e., molecules that contain an antigen binding site which specifically binds an antigen, such as Tango-77. A molecule which specifically binds to Tango-77 is a molecule which binds Tango-77, but does not substantially bind other molecules in a sample, e.g., a  
35 biological sample, which naturally contains Tango-77.

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Examples of immunologically active portions of immunoglobulin molecules include F(ab) and F(ab')<sub>2</sub> fragments which can be generated by treating the antibody with an enzyme such as pepsin. The invention provides polyclonal and monoclonal antibodies that bind Tango-77. The term "monoclonal antibody" or "monoclonal antibody composition", as used herein, refers to a population of antibody molecules that contain only one species of an antigen binding site capable of immunoreacting with a particular epitope of Tango-77. A monoclonal antibody composition thus typically displays a single binding affinity for a particular Tango-77 protein with which it immunoreacts.

Polyclonal anti-Tango-77 antibodies can be prepared as described above by immunizing a suitable subject with a Tango-77 immunogen. The anti-Tango-77 antibody titer in the immunized subject can be monitored over time by standard techniques, such as with an enzyme linked immunosorbent assay (ELISA) using immobilized Tango-77. If desired, the antibody molecules directed against Tango-77 can be isolated from the mammal (e.g., from the blood) and further purified by well-known techniques, such as protein A chromatography to obtain the IgG fraction. At an appropriate time after immunization, e.g., when the anti-Tango-77 antibody titers are highest, antibody-producing cells can be obtained from the subject and used to prepare monoclonal antibodies by standard techniques, such as the hybridoma technique originally described by Kohler and Milstein (1975) *Nature* 256:495-497, the human B cell hybridoma technique (Kozbor et al. (1983) *Immunol Today* 4:72), the EBV-hybridoma technique (Cole et al. (1985), *Monoclonal Antibodies and Cancer Therapy*, Alan R. Liss, Inc., pp. 77-96) or trioma techniques. The technology for producing hybridomas is well known (see generally Current

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Protocols in Immunology (1994) Coligan et al. (eds.) John Wiley & Sons, Inc., New York, NY). Briefly, an immortal cell line (typically a myeloma) is fused to lymphocytes (typically splenocytes) from a mammal immunized with a  
5 Tango-77 immunogen as described above, and the culture supernatants of the resulting hybridoma cells are screened to identify a hybridoma producing a monoclonal antibody that binds Tango-77.

Any of the many well known protocols used for  
10 fusing lymphocytes and immortalized cell lines can be applied for the purpose of generating an anti-Tango-77 monoclonal antibody (see, e.g., Current Protocols in Immunology, supra; Galfre et al. (1977) *Nature* 266:55052; R.H. Kenneth, in *Monoclonal Antibodies: A New Dimension*  
15 *In Biological Analyses*, Plenum Publishing Corp., New York, New York (1980); and Lerner (1981) *Yale J. Biol. Med.*, 54:387-402. Moreover, the ordinarily skilled worker will appreciate that there are many variations of such methods which also would be useful. Typically, the  
20 immortal cell line (e.g., a myeloma cell line) is derived from the same mammalian species as the lymphocytes. For example, murine hybridomas can be made by fusing lymphocytes from a mouse immunized with an immunogenic preparation of the present invention with an immortalized  
25 mouse cell line, e.g., a myeloma cell line that is sensitive to culture medium containing hypoxanthine, aminopterin and thymidine ("HAT medium"). Any of a number of myeloma cell lines can be used as a fusion partner according to standard techniques, e.g., the P3-  
30 NS1/1-Ag4-1, P3-x63-Ag8.653 or Sp2/O-Ag14 myeloma lines. These myeloma lines are available from ATCC. Typically, HAT-sensitive mouse myeloma cells are fused to mouse splenocytes using polyethylene glycol ("PEG"). Hybridoma cells resulting from the fusion are then selected using  
35 HAT medium, which kills unfused and unproductively fused

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myeloma cells (unfused splenocytes die after several days because they are not transformed). Hybridoma cells producing a monoclonal antibody of the invention are detected by screening the hybridoma culture supernatants for antibodies that bind Tango-77, e.g., using a standard ELISA assay.

Alternative to preparing monoclonal antibody-secreting hybridomas, a monoclonal anti-Tango-77 antibody can be identified and isolated by screening a recombinant combinatorial immunoglobulin library (e.g., an antibody phage display library) with Tango-77 to thereby isolate immunoglobulin library members that bind Tango-77. Kits for generating and screening phage display libraries are commercially available (e.g., the Pharmacia Recombinant Phage Antibody System, Catalog No. 27-9400-01; and the Stratagene SurfZAP™ Phage Display Kit, Catalog No. 240612). Additionally, examples of methods and reagents particularly amenable for use in generating and screening antibody display library can be found in, for example, U.S. Patent No. 5,223,409; PCT Publication No. WO 92/18619; PCT Publication No. WO 91/17271; PCT Publication No. WO 92/20791; PCT Publication No. WO 92/15679; PCT Publication No. WO 93/01288; PCT Publication No. WO 92/01047; PCT Publication No. WO 92/09690; PCT Publication No. WO 90/02809; Fuchs et al. (1991) *Bio/Technology* 9:1370-1372; Hay et al. (1992) *Hum. Antibod. Hybridomas* 3:81-85; Huse et al. (1989) *Science* 246:1275-1281; Griffiths et al. (1993) *EMBO J* 12:725-734.

Additionally, recombinant anti-Tango-77 antibodies, such as chimeric and humanized monoclonal antibodies, comprising both human and non-human portions, which can be made using standard recombinant DNA techniques, are within the scope of the invention. Such chimeric and humanized monoclonal antibodies can be produced by recombinant DNA techniques known in the art,

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for example using methods described in PCT Publication No. WO 87/02671; European Patent Application 184,187; European Patent Application 171,496; European Patent Application 173,494; PCT Publication No. WO 86/01533; 5 U.S. Patent No. 4,816,567; European Patent Application 125,023; Better et al. (1988) *Science* 240:1041-1043; Liu et al. (1987) *Proc. Natl. Acad. Sci. USA* 84:3439-3443; Liu et al. (1987) *J. Immunol.* 139:3521-3526; Sun et al. (1987) *Proc. Natl. Acad. Sci. USA* 84:214-218; Nishimura 10 et al. (1987) *Canc. Res.* 47:999-1005; Wood et al. (1985) *Nature* 314:446-449; and Shaw et al. (1988) *J. Natl. Cancer Inst.* 80:1553-1559; Morrison (1985) *Science* 229:1202-1207; Oi et al. (1986) *Bio/Techniques* 4:214; U.S. Patent 5,225,539; Jones et al. (1986) *Nature* 15 321:552-525; Verhoeyan et al. (1988) *Science* 239:1534; and Beidler et al. (1988) *J. Immunol.* 141:4053-4060.

Completely human antibodies are particularly desirable for therapeutic treatment of human patients. Such antibodies can be produced using transgenic mice 20 which are incapable of expressing endogenous immunoglobulin heavy and light chains genes, but which can express human heavy and light chain genes. The transgenic mice are immunized in the normal fashion with a selected antigen, e.g., all or a portion of Tango-77. 25 Monoclonal antibodies directed against the antigen can be obtained using conventional hybridoma technology. The human immunoglobulin transgenes harbored by the transgenic mice rearrange during B cell differentiation, and subsequently undergo class switching and somatic 30 mutation. Thus, using such a technique, it is possible to produce therapeutically useful IgG, IgA and IgE antibodies. For an overview of this technology for producing human antibodies, see Lonberg and Huszar (1995, *Int. Rev. Immunol.* 13:65-93). For a detailed discussion 35 of this technology for producing human antibodies and

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human monoclonal antibodies and protocols for producing such antibodies, see, e.g., U.S. Patent 5,625,126; U.S. Patent 5,633,425; U.S. Patent 5,569,825; U.S. Patent 5,661,016; and U.S. Patent 5,545,806. In addition, 5 companies such as Abgenix, Inc. (Freemont, CA), can be engaged to provide human antibodies directed against a selected antigen using technology similar to the described above.

Completely human antibodies which recognize a 10 selected epitope can be generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody, e.g., a murine antibody, is used to guide the selection of a completely human antibody recognizing the same epitope.

15 First, a non-human monoclonal antibody which binds a selected antigen (epitope), e.g., an antibody which inhibits Tango-77 activity, is identified. The heavy chain and the light chain of the non-human antibody are cloned and used to create phage display Fab fragments. 20 For example, the heavy chain gene can be cloned into a plasmid vector so that the heavy chain can be secreted from bacteria. The light chain gene can be cloned into a phage coat protein gene so that the light chain can be expressed on the surface of phage. A repertoire (random 25 collection) of human light chains fused to phage is used to infect the bacteria which express the non-human heavy chain. The resulting progeny phage display hybrid antibodies (human light chain/non-human heavy chain). The selected antigen is used in a panning screen to 30 select phage which bind the selected antigen. Several rounds of selection may be required to identify such phage. Next, human light chain genes are isolated from the selected phage which bind the selected antigen. These selected human light chain genes are then used to 35 guide the selection of human heavy chain genes as

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follows. The selected human light chain genes are inserted into vectors for expression by bacteria. Bacteria expressing the selected human light chains are infected with a repertoire of human heavy chains fused to  
5 phage. The resulting progeny phage display human antibodies (human light chain/human heavy chain).

Next, the selected antigen is used in a panning screen to select phage which bind the selected antigen. The phage selected in this step display completely human  
10 antibody which recognize the same epitope recognized by the original selected, non-human monoclonal antibody. The genes encoding both the heavy and light chains are readily isolated and be further manipulated for production of human antibody. This technology is  
15 described by Jespers et al. (1994, *Bio/technology* 12:899-903).

An anti-Tango-77 antibody (e.g., monoclonal antibody) can be used to isolate Tango-77 by standard techniques, such as affinity chromatography or  
20 immunoprecipitation. An anti-Tango-77 antibody can facilitate the purification of natural Tango-77 from cells and of recombinantly produced Tango-77 expressed in host cells. Moreover, an anti-Tango-77 antibody can be used to detect Tango-77 protein (e.g., in a cellular  
25 lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the Tango-77 protein. Anti-Tango-77 antibodies can be used diagnostically to monitor protein levels in tissue as part of a clinical testing procedure, e.g., to, for  
30 example, determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials,  
35 bioluminescent materials, and radioactive materials.



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Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase,  $\beta$ -galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and  
5 avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example  
10 of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{35}\text{S}$  or  $^3\text{H}$ .

### III. Recombinant Expression Vectors and Host Cells

Another aspect of the invention pertains to  
15 vectors, preferably expression vectors, containing a nucleic acid molecule encoding Tango-77 (or a portion thereof). As used herein, the term "vector" refers to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of  
20 vector is a "plasmid", which refers to a circular double stranded DNA loop into which additional DNA segments can be ligated. Another type of vector is a viral vector, wherein additional DNA segments can be ligated into the viral genome. Certain vectors are capable of autonomous  
25 replication in a host cell into which they are introduced (e.g., bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (e.g., non-episomal mammalian vectors) are integrated into the genome of a host cell upon  
30 introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors, expression vectors, are capable of directing the expression of genes to which they are operably linked. In general, expression vectors of utility in recombinant

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DNA techniques are often in the form of plasmids (vectors). However, the invention is intended to include such other forms of expression vectors, such as viral vectors (e.g., replication defective retroviruses, adenoviruses and adeno-associated viruses), which serve equivalent functions.

The recombinant expression vectors of the invention comprise a nucleic acid of the invention in a form suitable for expression of the nucleic acid in a host cell, which means that the recombinant expression vectors include one or more regulatory sequences, selected on the basis of the host cells to be used for expression, which is operably linked to the nucleic acid sequence to be expressed. Within a recombinant expression vector, "operably linked" is intended to mean that the nucleotide sequence of interest is linked to the regulatory sequence(s) in a manner which allows for expression of the nucleotide sequence (e.g., in an in vitro transcription/translation system or in a host cell when the vector is introduced into the host cell). The term "regulatory sequence" is intended to include promoters, enhancers and other expression control elements (e.g., polyadenylation signals). Such regulatory sequences are described, for example, in Goeddel; *Gene Expression Technology: Methods in Enzymology* 185, Academic Press, San Diego, CA (1990). Regulatory sequences include those which direct constitutive expression of a nucleotide sequence in many types of host cell and those which direct expression of the nucleotide sequence only in certain host cells (e.g., tissue-specific regulatory sequences). It will be appreciated by those skilled in the art that the design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of protein desired, etc. The expression

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vectors of the invention can be introduced into host cells to thereby produce proteins or peptides, including fusion proteins or peptides, encoded by nucleic acids as described herein (e.g., Tango-77 proteins, mutant forms of Tango-77, fusion proteins, etc.).

The recombinant expression vectors of the invention can be designed for expression of Tango-77 in prokaryotic or eukaryotic cells, e.g., bacterial cells such as *E. coli*, insect cells (using baculovirus expression vectors), yeast cells or mammalian cells. Suitable host cells are discussed further in Goeddel, *Gene Expression Technology: Methods in Enzymology* 185, Academic Press, San Diego, CA (1990). Alternatively, the recombinant expression vector can be transcribed and translated in vitro, for example using T7 promoter regulatory sequences and T7 polymerase.

Expression of proteins in prokaryotes is most often carried out in *E. coli* with vectors containing constitutive or inducible promoters directing the expression of either fusion or non-fusion proteins. Fusion vectors add a number of amino acids to a protein encoded therein, usually to the amino terminus of the recombinant protein. Such fusion vectors typically serve three purposes: 1) to increase expression of recombinant protein; 2) to increase the solubility of the recombinant protein; and 3) to aid in the purification of the recombinant protein by acting as a ligand in affinity purification. Often, in fusion expression vectors, a proteolytic cleavage site is introduced at the junction of the fusion moiety and the recombinant protein to enable separation of the recombinant protein from the fusion moiety subsequent to purification of the fusion protein. Such enzymes, and their cognate recognition sequences, include Factor Xa, thrombin and enterokinase. Typical fusion expression vectors include pGEX (Pharmacia

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Biotech Inc; Smith and Johnson (1988) *Gene* 67:31-40), pMAL (New England Biolabs, Beverly, MA) and pRIT5 (Pharmacia, Piscataway, NJ) which fuse glutathione S-transferase (GST), maltose E binding protein, or protein A, respectively, to the target recombinant protein.

Examples of suitable inducible non-fusion *E. coli* expression vectors include pTrc (Amann et al. (1988) *Gene* 69:301-315) and pET 11d (Studier et al., *Gene Expression Technology: Methods in Enzymology* 185, Academic Press, San Diego, California (1990) 60-89). Target gene expression from the pTrc vector relies on host RNA polymerase transcription from a hybrid trp-lac fusion promoter. Target gene expression from the pET 11d vector relies on transcription from a T7 *gn10*-lac fusion promoter mediated by a coexpressed viral RNA polymerase (T7 *gn1*). This viral polymerase is supplied by host strains BL21(DE3) or HMS174(DE3) from a resident  $\lambda$  prophage harboring a T7 *gn1* gene under the transcriptional control of the lacUV 5 promoter.

One strategy to maximize recombinant protein expression in *E. coli* is to express the protein in a host bacteria with an impaired capacity to proteolytically cleave the recombinant protein (Gottesman, *Gene Expression Technology: Methods in Enzymology* 185, Academic Press, San Diego, California (1990) 119-128). Another strategy is to alter the nucleic acid sequence of the nucleic acid to be inserted into an expression vector so that the individual codons for each amino acid are those preferentially utilized in *E. coli* (Wada et al. (1992) *Nucleic Acids Res.* 20:2111-2118). Such alteration of nucleic acid sequences of the invention can be carried out by standard DNA synthesis techniques.

In another embodiment, the Tango-77 expression vector is a yeast expression vector. Examples of vectors for expression in yeast *S. cerevisiae* include pYepSec1

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(Baldari et al. (1987) *EMBO J.* 6:229-234), pMFa (Kurjan and Herskowitz (1982) *Cell* 30:933-943), pJRY88 (Schultz et al. (1987) *Gene* 54:113-123), pYES2 (Invitrogen Corporation, San Diego, CA), and picZ (Invitrogen Corp, 5 San Diego, CA).

Alternatively, Tango-77 can be expressed in insect cells using baculovirus expression vectors. Baculovirus vectors available for expression of proteins in cultured insect cells (e.g., Sf 9 cells) include the pAc series 10 (Smith et al. (1983) *Mol. Cell Biol.* 3:2156-2165) and the pVL series (Lucklow and Summers (1989) *Virology* 170:31-39).

In yet another embodiment, a nucleic acid of the invention is expressed in mammalian cells using a 15 mammalian expression vector. Examples of mammalian expression vectors include pCDM8 (Seed (1987) *Nature* 329:840) and pMT2PC (Kaufman et al. (1987) *EMBO J.* 6:187-195). When used in mammalian cells, the expression vector's control functions are often provided by viral 20 regulatory elements. For example, commonly used promoters are derived from polyoma, Adenovirus 2, cytomegalovirus and Simian Virus 40. For other suitable expression systems for both prokaryotic and eukaryotic cells see chapters 16 and 17 of Sambrook et al. (*supra*).

25 In another embodiment, the recombinant mammalian expression vector is capable of directing expression of the nucleic acid preferentially in a particular cell type (e.g., tissue-specific regulatory elements are used to express the nucleic acid). Tissue-specific regulatory 30 elements are known in the art. Non-limiting examples of suitable tissue-specific promoters include the albumin promoter (liver-specific; Pinkert et al. (1987) *Genes Dev.* 1:268-277), lymphoid-specific promoters (Calame and Eaton (1988) *Adv. Immunol.* 43:235-275), in particular 35 promoters of T cell receptors (Winoto and Baltimore

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(1989) *EMBO J.* 8:729-733) and immunoglobulins (Banerji et al. (1983) *Cell* 33:729-740; Queen and Baltimore (1983) *Cell* 33:741-748), neuron-specific promoters (e.g., the neurofilament promoter; Byrne and Ruddle (1989) *Proc. Natl. Acad. Sci. USA* 86:5473-5477), pancreas-specific promoters (Edlund et al. (1985) *Science* 230:912-916), and mammary gland-specific promoters (e.g., milk whey promoter; U.S. Patent No. 4,873,316 and European Application Publication No. 264,166). Developmentally-regulated promoters are also encompassed, for example the murine hox promoters (Kessel and Gruss (1990) *Science* 249:374-379) and the  $\alpha$ -fetoprotein promoter (Campes and Tilghman (1989) *Genes Dev.* 3:537-546).

The invention further provides a recombinant expression vector comprising a DNA molecule of the invention cloned into the expression vector in an antisense orientation. That is, the DNA molecule is operably linked to a regulatory sequence in a manner which allows for expression (by transcription of the DNA molecule) of an RNA molecule which is antisense to Tango-77 mRNA. Regulatory sequences operably linked to a nucleic acid cloned in the antisense orientation can be chosen which direct the continuous expression of the antisense RNA molecule in a variety of cell types, for instance viral promoters and/or enhancers, or regulatory sequences can be chosen which direct constitutive, tissue specific or cell type specific expression of antisense RNA. The antisense expression vector can be in the form of a recombinant plasmid, phagemid or attenuated virus in which antisense nucleic acids are produced under the control of a high efficiency regulatory region, the activity of which can be determined by the cell type into which the vector is introduced. For a discussion of the regulation of gene expression using antisense genes see

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Weintraub et al. (Reviews - Trends in Genetics, Vol. 1(1) 1986).

Another aspect of the invention pertains to host cells into which a recombinant expression vector of the invention has been introduced. The terms "host cell" and "recombinant host cell" are used interchangeably herein. It is understood that such terms refer not only to the particular subject cell but to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

A host cell can be any prokaryotic or eukaryotic cell. For example, Tango-77 protein can be expressed in bacterial cells such as *E. coli*, insect cells, yeast or mammalian cells (such as Chinese hamster ovary cells (CHO) or COS cells). Other suitable host cells are known to those skilled in the art.

Vector DNA can be introduced into prokaryotic or eukaryotic cells via conventional transformation or transfection techniques. As used herein, the terms "transformation" and "transfection" are intended to refer to a variety of art-recognized techniques for introducing foreign nucleic acid (e.g., DNA) into a host cell, including calcium phosphate or calcium chloride coprecipitation, DEAE-dextran-mediated transfection, lipofection, or electroporation. Suitable methods for transforming or transfecting host cells can be found in Sambrook, et al. (*supra*), and other laboratory manuals.

For stable transfection of mammalian cells, it is known that, depending upon the expression vector and transfection technique used, only a small fraction of cells may integrate the foreign DNA into their genome.

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In order to identify and select these integrants, a gene that encodes a selectable marker (e.g., for resistance to antibiotics) is generally introduced into the host cells along with the gene of interest. Preferred selectable  
5 markers include those which confer resistance to drugs, such as G418, hygromycin and methotrexate. Nucleic acid encoding a selectable marker can be introduced into a host cell on the same vector as that encoding Tango-77 or can be introduced on a separate vector. Cells stably  
10 transfected with the introduced nucleic acid can be identified by drug selection (e.g., cells that have incorporated the selectable marker gene will survive, while the other cells die).

A host cell of the invention, such as a  
15 prokaryotic or eukaryotic host cell in culture, can be used to produce (i.e., express) Tango-77 protein. Accordingly, the invention further provides methods for producing Tango-77 protein using the host cells of the invention. In one embodiment, the method comprises  
20 culturing the host cell of invention (into which a recombinant expression vector encoding Tango-77 has been introduced) in a suitable medium such that Tango-77 protein is produced. In another embodiment, the method further comprises isolating Tango-77 from the medium or  
25 the host cell.

The host cells of the invention can also be used to produce nonhuman transgenic animals. For example, in one embodiment, a host cell of the invention is a fertilized oocyte or an embryonic stem cell into which  
30 Tango-77-coding sequences have been introduced. Such host cells can then be used to create non-human transgenic animals in which exogenous Tango-77 sequences have been introduced into their genome or homologous recombinant animals in which endogenous Tango-77  
35 sequences have been altered. Such animals are useful for



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studying the function and/or activity of Tango-77 and for identifying and/or evaluating modulators of Tango-77 activity. As used herein, a "transgenic animal" is a non-human animal, preferably a mammal, more preferably a rodent such as a rat or mouse, in which one or more of the cells of the animal includes a transgene. Other examples of transgenic animals include non-human primates, sheep, dogs, cows, goats, chickens, amphibians, etc. A transgene is exogenous DNA which is integrated into the genome of a cell from which a transgenic animal develops and which remains in the genome of the mature animal, thereby directing the expression of an encoded gene product in one or more cell types or tissues of the transgenic animal. As used herein, an "homologous recombinant animal" is a non-human animal, preferably a mammal, more preferably a mouse, in which an endogenous Tango-77 gene has been altered by homologous recombination between the endogenous gene and an exogenous DNA molecule introduced into a cell of the animal, e.g., an embryonic cell of the animal, prior to development of the animal.

A transgenic animal of the invention can be created by introducing Tango-77-encoding nucleic acid into the male pronuclei of a fertilized oocyte, e.g., by microinjection, retroviral infection, and allowing the oocyte to develop in a pseudopregnant female foster animal. The Tango-77 cDNA sequence e.g., that of (SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6; SEQ ID NO:10 or the cDNA of ATCC 98807) can be introduced as a transgene into the genome of a non-human animal. Alternatively, a nonhuman homologue of the human Tango-77 gene, such as a mouse Tango-77 gene, can be isolated based on hybridization to the human Tango-77 cDNA and used as a transgene. Intronic sequences and polyadenylation signals can also be included in the transgene to increase the efficiency

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of expression of the transgene. A tissue-specific regulatory sequence(s) can be operably linked to the Tango-77 transgene to direct expression of Tango-77 protein to particular cells. Methods for generating transgenic animals via embryo manipulation and microinjection, particularly animals such as mice, have become conventional in the art and are described, for example, in U.S. Patent Nos. 4,736,866 and 4,870,009, U.S. Patent No. 4,873,191 and in Hogan, *Manipulating the Mouse Embryo* (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1986). Similar methods are used for production of other transgenic animals. A transgenic founder animal can be identified based upon the presence of the Tango-77 transgene in its genome and/or expression of Tango-77 mRNA in tissues or cells of the animals. A transgenic founder animal can then be used to breed additional animals carrying the transgene. Moreover, transgenic animals carrying a transgene encoding Tango-77 can further be bred to other transgenic animals carrying other transgenes.

To create an homologous recombinant animal, a vector is prepared which contains at least a portion of a Tango-77 gene (e.g., a human or a non-human homolog of the Tango-77 gene, e.g., a murine Tango-77 gene) into which a deletion, addition or substitution has been introduced to thereby alter, e.g., functionally disrupt, the Tango-77 gene. In a preferred embodiment, the vector is designed such that, upon homologous recombination, the endogenous Tango-77 gene is functionally disrupted (i.e., no longer encodes a functional protein; also referred to as a "knock out" vector). Alternatively, the vector can be designed such that, upon homologous recombination, the endogenous Tango-77 gene is mutated or otherwise altered but still encodes functional protein (e.g., the upstream regulatory region can be altered to thereby

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alter the expression of the endogenous Tango-77 protein). In the homologous recombination vector, the altered portion of the Tango-77 gene is flanked at its 5' and 3' ends by additional nucleic acid of the Tango-77 gene to  
5 allow for homologous recombination to occur between the exogenous Tango-77 gene carried by the vector and an endogenous Tango-77 gene in an embryonic stem cell. The additional flanking Tango-77 nucleic acid is of sufficient length for successful homologous recombination  
10 with the endogenous gene. Typically, several kilobases of flanking DNA (both at the 5' and 3' ends) are included in the vector (see, e.g., Thomas and Capecchi (1987) *Cell* 51:503 for a description of homologous recombination vectors). The vector is introduced into an embryonic  
15 stem cell line (e.g., by electroporation) and cells in which the introduced Tango-77 gene has homologously recombined with the endogenous Tango-77 gene are selected (see, e.g., Li et al. (1992) *Cell* 69:915). The selected cells are then injected into a blastocyst of an animal  
20 (e.g., a mouse) to form aggregation chimeras (see, e.g., Bradley in *Teratocarcinomas and Embryonic Stem Cells: A Practical Approach*, Robertson, ed. (IRL, Oxford, 1987) pp. 113-152). A chimeric embryo can then be implanted into a suitable pseudopregnant female foster animal and  
25 the embryo brought to term. Progeny harboring the homologously recombined DNA in their germ cells can be used to breed animals in which all cells of the animal contain the homologously recombined DNA by germline transmission of the transgene. Methods for constructing  
30 homologous recombination vectors and homologous recombinant animals are described further in Bradley (1991) *Current Opinion in Bio/Technology* 2:823-829 and in PCT Publication Nos. WO 90/11354, WO 91/01140, WO 92/0968, and WO 93/04169.

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In another embodiment, transgenic non-human animals can be produced which contain selected systems which allow for regulated expression of the transgene. One example of such a system is the *cre/loxP* recombinase system of bacteriophage P1. For a description of the *cre/loxP* recombinase system, see, e.g., Lakso et al. (1992) *Proc. Natl. Acad. Sci. USA* 89:6232-6236. Another example of a recombinase system is the FLP recombinase system of *Saccharomyces cerevisiae* (O'Gorman et al. (1991) *Science* 251:1351-1355. If a *cre/loxP* recombinase system is used to regulate expression of the transgene, animals containing transgenes encoding both the Cre recombinase and a selected protein are required. Such animals can be provided through the construction of "double" transgenic animals, e.g., by mating two transgenic animals, one containing a transgene encoding a selected protein and the other containing a transgene encoding a recombinase.

Clones of the non-human transgenic animals described herein can also be produced according to the methods described in Wilmut et al. (1997) *Nature* 385:810-813 and PCT Publication Nos. WO 97/07668 and WO 97/07669. In brief, a cell, e.g., a somatic cell, from the transgenic animal can be isolated and induced to exit the growth cycle and enter G<sub>0</sub> phase. The quiescent cell can then be fused, e.g., through the use of electrical pulses, to an enucleated oocyte from an animal of the same species from which the quiescent cell is isolated. The reconstructed oocyte is then cultured such that it develops to morula or blastocyte and then transferred to pseudopregnant female foster animal. The offspring borne of this female foster animal will be a clone of the animal from which the cell, e.g., the somatic cell, is isolated.

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#### IV. Pharmaceutical Compositions

The Tango-77 nucleic acid molecules, Tango-77 proteins, and anti-Tango-77 antibodies (also referred to herein as "active compounds") of the invention can be  
5 incorporated into pharmaceutical compositions suitable for administration. Such compositions typically comprise the nucleic acid molecule, protein, or antibody and a pharmaceutically acceptable carrier. As used herein the  
10 language "pharmaceutically acceptable carrier" is intended to include any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like, compatible with pharmaceutical administration. The use  
15 of such media and agents for pharmaceutically active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active compound, use thereof in the compositions is contemplated. Supplementary active compounds can also be incorporated into the compositions.

20 A pharmaceutical composition of the invention is formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral, (e.g. intravenous, intradermal, subcutaneous) (e.g., oral inhalation), transdermal  
25 (topical), transmucosal, and rectal administration. Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene  
30 glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as  
35 acetates, citrates or phosphates and agents for the

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adjustment of tonicity such as sodium chloride or dextrose. pH can be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. The parenteral preparation can be enclosed in ampoules, disposable  
5 syringes or multiple dose vials made of glass or plastic.

Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable  
10 solutions or dispersions. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL™ (BASF; Parsippany, NJ) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be  
15 fluid to the extent that easy syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing,  
20 for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance  
25 of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid,  
30 thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as mannitol, sorbitol, sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including

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in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

Sterile injectable solutions can be prepared by incorporating the active compound (e.g., a Tango-77 protein or anti-Tango-77 antibody) in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle which contains a basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum drying and freeze-drying which yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

Oral compositions generally include an inert diluent or an edible carrier. They can be enclosed in gelatin capsules or compressed into tablets. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form of tablets, troches, or capsules. Oral compositions can also be prepared using a fluid carrier for use as a mouthwash, wherein the compound in the fluid carrier is applied orally and swished and expectorated or swallowed. Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition. The tablets, pills, capsules, troches and the like can contain any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or Sterotes; a

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glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

5 For administration by inhalation, the compounds are delivered in the form of an aerosol spray from a pressurized container or dispenser which contains a suitable propellant, e.g., a gas such as carbon dioxide, or a nebulizer.

10 Systemic administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and  
15 include, for example, for transmucosal administration, detergents, bile salts, and fusidic acid derivatives. Transmucosal administration can be accomplished through the use of nasal sprays or suppositories. For  
transdermal administration, the active compounds are  
20 formulated into ointments, salves, gels, or creams as generally known in the art.

The compounds can also be prepared in the form of suppositories (e.g., with conventional suppository bases such as cocoa butter and other glycerides) or retention  
25 enemas for rectal delivery.

In one embodiment, the active compounds are prepared with carriers that will protect the compound against rapid elimination from the body, such as a controlled release formulation, including implants and  
30 microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Methods for preparation of such formulations will be apparent to  
35 those skilled in the art. The materials can also be



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obtained commercially from Alza Corporation and Nova Pharmaceuticals, Inc. Liposomal suspensions (including liposomes targeted to infected cells with monoclonal antibodies to viral antigens) can also be used as  
5 pharmaceutically acceptable carriers. These can be prepared according to methods known to those skilled in the art, for example, as described in U.S. Patent No. 4,522,811.

It is especially advantageous to formulate oral or  
10 parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the subject to be treated; each unit containing a predetermined quantity of active  
15 compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the dosage unit forms of the invention are dictated by and directly dependent on the unique characteristics of the active compound and the  
20 particular therapeutic effect to be achieved, and the limitations inherent in the art of compounding such an active compound for the treatment of individuals.

The nucleic acid molecules of the invention can be inserted into vectors and used as gene therapy vectors.  
25 Gene therapy vectors can be delivered to a subject by, for example, intravenous injection, local administration (U.S. Patent 5,328,470) or by stereotactic injection (see, e.g., Chen et al. (1994) *Proc. Natl. Acad. Sci. USA* 91:3054-3057). The pharmaceutical preparation of the  
30 gene therapy vector can include the gene therapy vector in an acceptable diluent, or can comprise a slow release matrix in which the gene delivery vehicle is imbedded. Alternatively, where the complete gene delivery vector can be produced intact from recombinant cells, e.g.  
35 retroviral vectors, the pharmaceutical preparation can

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include one or more cells which produce the gene delivery system.

The pharmaceutical compositions can be included in a container, pack, or dispenser together with instructions for administration.

#### V. Uses and Methods of the Invention

The nucleic acid molecules, proteins, protein homologues, and antibodies described herein can be used in one or more of the following methods: a) screening assays; b) detection assays (e.g., chromosomal mapping, tissue typing, forensic biology); c) predictive medicine (e.g., diagnostic assays, prognostic assays, monitoring clinical trials, and pharmacogenomics); and d) methods of treatment (e.g., therapeutic and prophylactic). A Tango-77 protein interacts with other cellular proteins and can thus be used for regulation of inflammation. The polypeptides of the invention can be used in assays to determine biological activity. For example, they could be used in a panel of proteins for high-throughput screening.

The isolated nucleic acid molecules of the invention can be used to express Tango-77 protein (e.g., via a recombinant expression vector in a host cell in gene therapy applications), to detect Tango-77 mRNA (e.g., in a biological sample) or a genetic lesion in a Tango-77 gene, and to modulate Tango-77 activity. In addition, the Tango-77 proteins can be used to screen drugs or compounds which modulate the Tango-77 activity or expression as well as to treat disorders characterized by insufficient or excessive production of Tango-77 protein or production of Tango-77 protein forms which have decreased or aberrant activity compared to Tango-77 wild type protein. In addition, the anti-Tango-77

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antibodies of the invention can be used to detect and isolate Tango-77 proteins and modulate Tango-77 activity.

This invention further pertains to novel agents identified by the above-described screening assays and  
5 uses thereof for treatments as described herein.

#### A. Screening Assays

The invention provides a method (also referred to herein as a "screening assay") for identifying modulators, i.e., candidate or test compounds or agents  
10 (e.g., peptides, peptidomimetics, small molecules or other drugs) which bind to Tango-77 proteins or have a stimulatory or inhibitory effect on, for example, Tango-77 expression or Tango-77 activity.

Examples of methods for the synthesis of molecular  
15 libraries can be found in the art, for example in:  
DeWitt et al. (1993) *Proc. Natl. Acad. Sci. USA* 90:6909;  
Erb et al. (1994) *Proc. Natl. Acad. Sci. USA* 91:11422;  
Zuckermann et al. (1994). *J. Med. Chem.* 37:2678; Cho et  
al. (1993) *Science* 261:1303; Carrell et al. (1994) *Angew.*  
20 *Chem. Int. Ed. Engl.* 33:2059; Carell et al. (1994) *Angew.*  
*Chem. Int. Ed. Engl.* 33:2061; and Gallop et al. (1994) *J.*  
*Med. Chem.* 37:1233.

Libraries of compounds may be presented in solution (e.g., Houghten (1992) *Bio/Techniques* 13:412-  
25 421), or on beads (Lam (1991) *Nature* 354:82-84), chips (Fodor (1993) *Nature* 364:555-556), bacteria (U.S. Patent No. 5,223,409), spores (Patent Nos. 5,571,698; 5,403,484; and 5,223,409), plasmids (Cull et al. (1992) *Proc. Natl. Acad. Sci. USA* 89:1865-1869) or phage (Scott and Smith  
30 (1990) *Science* 249:386-390; Devlin (1990) *Science* 249:404-406; Cwirla et al. (1990) *Proc. Natl. Acad. Sci. USA* 87:6378-6382; and Felici (1991) *J. Mol. Biol.* 222:301-310).

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In another embodiment, an assay is used to determine the ability of the test compound to modulate the activity of Tango-77 or a biologically active portion thereof, for example, by determining the ability of the  
5 Tango-77 protein to bind to or interact with a Tango-77 target molecule. As used herein, a "target molecule" is a molecule with which a Tango-77 protein binds or interacts in nature, for example, a molecule on the surface of a cell. A Tango-77 target molecule can be a  
10 non-Tango-77 molecule or a Tango-77 protein or polypeptide of the present invention. In one embodiment, a Tango-77 target molecule is a component of a signal transduction pathway, for example, Tango-77 may bind to a IL-1 receptor or another receptor thereby blocking the  
15 receptor and inhibiting future signal transduction. Determining the ability of the Tango-77 protein to bind to or interact with a Tango-77 target molecule can be accomplished by one of the methods described above. In a preferred embodiment, determining the ability of the  
20 Tango-77 protein to bind to or interact with a Tango-77 target molecule can be accomplished by determining the activity of the target molecule. For example, the activity of the target molecule can be determined by detecting induction of a cellular second messenger of the  
25 target (e.g., intracellular  $\text{Ca}^{2+}$ , diacylglycerol, IP3, etc.), detecting catalytic/enzymatic activity of the target on an appropriate substrate, detecting the induction of a reporter gene (e.g., a Tango-77-responsive regulatory element operably linked to a nucleic acid  
30 encoding a detectable marker, e.g. luciferase), or detecting a cellular response, for example, inflammation.

In yet another embodiment, an assay of the present invention is a cell-free assay comprising contacting a  
Tango-77 protein or biologically active portion thereof  
35 with a test compound and determining the ability of the

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test compound to bind to the Tango-77 protein or biologically active portion thereof. Binding of the test compound to the Tango-77 protein can be determined either directly or indirectly as described above. In a preferred embodiment, the assay includes contacting the Tango-77 protein or biologically active portion thereof with a known compound which binds Tango-77 to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with a Tango-77 protein, wherein determining the ability of the test compound to interact with a Tango-77 protein comprises determining the ability of the test compound to preferentially bind to Tango-77 or biologically active portion thereof as compared to the known compound.

In another embodiment, an assay is a cell-free assay comprising contacting Tango-77 protein or biologically active portion thereof with a test compound and determining the ability of the test compound to modulate (e.g., stimulate or inhibit) the activity of the Tango-77 protein or biologically active portion thereof. Determining the ability of the test compound to modulate the activity of Tango-77 can be accomplished, for example, by determining the ability of the Tango-77 protein to bind to a Tango-77 target molecule by one of the methods described above for determining direct binding. In an alternative embodiment, determining the ability of the test compound to modulate the activity of Tango-77 can be accomplished by determining the ability of the Tango-77 protein to further modulate a Tango-77 target molecule. For example, the catalytic/enzymatic activity of the target molecule on an appropriate substrate can be determined as previously described.

In yet another embodiment, the cell-free assay comprises contacting the Tango-77 protein or biologically

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active portion thereof with a known compound which binds Tango-77 to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with a Tango-77 protein, wherein determining the ability of the test compound to interact with a Tango-77 protein comprises determining the ability of the Tango-77 protein to preferentially bind to or modulate the activity of a Tango-77 target molecule.

10 It is possible that membrane-bound forms of Tango-77 exist. The cell-free assays of the present invention are amenable to use of both the forms Tango-77. In the case of cell-free assays comprising a membrane-bound form of Tango-77, it may be desirable to utilize a  
15 solubilizing agent such that the membrane-bound form of Tango-77 is maintained in solution. Examples of such solubilizing agents include non-ionic detergents such as n-octylglucoside, n-dodecylglucoside, n-dodecylmaltoside, octanoyl-N-methylglucamide, decanoyl-N-methylglucamide,  
20 Triton® X-100, Triton® X-114, Thesit®, Isotridecypoly(ethylene glycol ether)n, 3-[(3-cholamidopropyl)dimethylamminio]-1-propane sulfonate (CHAPS), 3-[(3-cholamidopropyl)dimethylamminio]-2-hydroxy-1-propane sulfonate (CHAPSO), or N-dodecyl=N,N-dimethyl-3-ammonio-1-propane sulfonate.  
25

In more than one embodiment of the above assay methods of the present invention, it may be desirable to immobilize either Tango-77 or its target molecule to facilitate separation of complexed from uncomplexed forms  
30 of one or both of the proteins, as well as to accommodate automation of the assay. Binding of a test compound to Tango-77, or interaction of Tango-77 with a target molecule in the presence and absence of a candidate compound, can be accomplished in any vessel suitable for  
35 containing the reactants. Examples of such vessels

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include microtitre plates, test tubes, and micro-centrifuge tubes. In one embodiment, a fusion protein can be provided which adds a domain that allows one or both of the proteins to be bound to a matrix. For  
5 example, glutathione-S-transferase/ Tango-77 fusion proteins or glutathione-S-transferase/target fusion proteins can be adsorbed onto glutathione sepharose beads (Sigma Chemical Co.; St. Louis, MO) or glutathione derivatized microtitre plates, which are then combined  
10 with the test compound or the test compound and either the non-adsorbed target protein or Tango-77 protein, and the mixture incubated under conditions conducive to complex formation (e.g., at physiological conditions for salt and pH). Following incubation, the beads or  
15 microtitre plate wells are washed to remove any unbound components and complex formation is measured either directly or indirectly, for example, as described above. Alternatively, the complexes can be dissociated from the matrix, and the level of Tango-77 binding or activity  
20 determined using standard techniques.

Other techniques for immobilizing proteins on matrices can also be used in the screening assays of the invention. For example, either Tango-77 or its target molecule can be immobilized utilizing conjugation of  
25 biotin and streptavidin. Biotinylated Tango-77 or target molecules can be prepared from biotin-NHS (N-hydroxy-succinimide) using techniques well known in the art (e.g., biotinylation kit, Pierce Chemicals; Rockford, IL), and immobilized in the wells of streptavidin-coated  
30 96 well plates (Pierce Chemical). Alternatively, antibodies reactive with Tango-77 or target molecules but which do not interfere with binding of the Tango-77 protein to its target molecule can be derivatized to the wells of the plate, and unbound target or Tango-77  
35 trapped in the wells by antibody conjugation. Methods

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for detecting such complexes, in addition to those described above for the GST-immobilized complexes, include immunodetection of complexes using antibodies reactive with the Tango-77 or target molecule, as well as  
5 enzyme-linked assays which rely on detecting an enzymatic activity associated with the Tango-77 or target molecule.

In another embodiment, modulators of Tango-77 expression are identified in a method in which a cell is contacted with a candidate compound and the expression of  
10 Tango-77 mRNA or protein in the cell is determined. The level of expression of Tango-77 mRNA or protein in the presence of the candidate compound is compared to the level of expression of Tango-77 mRNA or protein in the absence of the candidate compound. The candidate  
15 compound can then be identified as a modulator of Tango-77 expression based on this comparison. For example, when expression of Tango-77 mRNA or protein is greater (statistically significantly greater) in the presence of the candidate compound than in its absence,  
20 the candidate compound is identified as a stimulator of Tango-77 mRNA or protein expression. Alternatively, when expression of Tango-77 mRNA or protein is less (statistically significantly less) in the presence of the candidate compound than in its absence, the candidate  
25 compound is identified as an inhibitor of Tango-77 mRNA or protein expression. The level of Tango-77 mRNA or protein expression in the cells can be determined by methods described herein for detecting Tango-77 mRNA or protein.

30 In yet another aspect of the invention, the Tango-77 proteins can be used as "bait proteins" in a two-hybrid assay or three hybrid assay (see, e.g., U.S. Patent No. 5,283,317; Zervos et al. (1993) *Cell* 72:223-232; Madura et al. (1993) *J. Biol. Chem.* 268:12046-12054;  
35 Bartel et al. (1993) *Bio/Techniques* 14:920-924; Iwabuchi



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et al. (1993) *Oncogene* 8:1693-1696; and PCT Publication No. WO 94/10300), to identify other proteins, which bind to or interact with Tango-77 ("Tango-77-binding proteins" or "Tango-77-bp") and modulate Tango-77 activity. Such  
5 Tango-77-binding proteins are also likely to be involved in the propagation of signals by the Tango-77 proteins as, for example, upstream or downstream elements of the Tango-77 pathway.

The two-hybrid system is based on the modular  
10 nature of most transcription factors, which consist of separable DNA-binding and activation domains. Briefly, the assay utilizes two different DNA constructs. In one construct, the gene that codes for Tango-77 is fused to a gene encoding the DNA binding domain of a known  
15 transcription factor (e.g., GAL-4). In the other construct, a DNA sequence, from a library of DNA sequences, that encodes an unidentified protein ("prey" or "sample") is fused to a gene that codes for the activation domain of the known transcription factor. If  
20 the "bait" and the "prey" proteins are able to interact, in vivo, forming an Tango-77-dependent complex, the DNA-binding and activation domains of the transcription factor are brought into close proximity. This proximity allows transcription of a reporter gene (e.g., LacZ)  
25 which is operably linked to a transcriptional regulatory site responsive to the transcription factor. Expression of the reporter gene can be detected and cell colonies containing the functional transcription factor can be isolated and used to obtain the cloned gene which encodes  
30 the protein which interacts with Tango-77.

This invention further pertains to novel agents identified by the above-described screening assays and uses thereof for treatments as described herein.

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## B. Detection Assays

Portions or fragments of the cDNA sequence identified herein (and the corresponding complete gene sequences) can be used in numerous ways as polynucleotide reagents. For example, the sequence can be used to: (i) map the respective gene on a chromosome and, thus, locate gene regions associated with genetic disease; (ii) identify an individual from a minute biological sample (tissue typing); and (iii) aid in forensic identification of a biological sample. These applications are described in the subsections below.

### 1. Chromosome Mapping

Once the sequence (or a portion of the sequence) of a gene has been isolated, this sequence can be used to map the location of the gene on a chromosome. Accordingly, Tango-77 nucleic acid molecules described herein or fragments thereof, can be used to map the location of the Tango-77 gene(s) on a chromosome. The mapping of the Tango-77 sequences to chromosomes is an important first step in correlating these sequences with genes associated with disease.

Briefly, a Tango-77 gene can be mapped to chromosomes by preparing PCR primers (preferably 15-25 bp in length) from the Tango-77 sequences. Computer analysis of Tango-77 sequences can be used to rapidly select primers that do not span more than one exon in the genomic DNA, thus complicating the amplification process. These primers can then be used for PCR screening of somatic cell hybrids containing individual human chromosomes. Only those hybrids containing the human gene corresponding to the Tango-77 sequences will yield an amplified fragment.

Somatic cell hybrids are prepared by fusing somatic cells from different mammals (e.g., human and

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mouse cells). As hybrids of human and mouse cells grow and divide, they gradually lose human chromosomes in random order, but retain the mouse chromosomes. By using media in which mouse cells cannot grow (because they lack a particular enzyme) but in which human cells can, the one human chromosome that contains the gene encoding the needed enzyme, will be retained. By using various media, panels of hybrid cell lines can be established. Each cell line in a panel contains either a single human chromosome or a small number of human chromosomes, and a full set of mouse chromosomes, allowing easy mapping of individual genes to specific human chromosomes. (D'Eustachio et al. (1983) *Science* 220:919-924). Somatic cell hybrids containing only fragments of human chromosomes can also be produced by using human chromosomes with translocations and deletions.

PCR mapping of somatic cell hybrids is a rapid procedure for assigning a particular sequence to a particular chromosome. Three or more sequences can be assigned per day using a single thermal cycler. Using the Tango-77 sequences to design oligonucleotide primers, sublocalization can be achieved with panels of fragments from specific chromosomes. Other mapping strategies which can similarly be used to map a Tango-77 sequence to its chromosome include *in situ* hybridization (described in Fan et al. (1990) *Proc. Natl. Acad. Sci. USA* 87:6223-27), pre-screening with labeled flow-sorted chromosomes, and pre-selection by hybridization to chromosome specific cDNA libraries.

Fluorescence *in situ* hybridization (FISH) of a DNA sequence to a metaphase chromosomal spread can further be used to provide a precise chromosomal location in one step. Chromosome spreads can be made using cells whose division has been blocked in metaphase by a chemical, e.g., colcemid that disrupts the mitotic spindle. The

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chromosomes can be treated briefly with trypsin, and then stained with Giemsa. A pattern of light and dark bands develops on each chromosome, so that the chromosomes can be identified individually. The FISH technique can be  
5 used with a DNA sequence as short as 500 or 600 bases. However, clones larger than 1,000 bases have a higher likelihood of binding to a unique chromosomal location with sufficient signal intensity for simple detection. Preferably 1,000 bases, and more preferably 2,000 bases  
10 will suffice to get good results at a reasonable amount of time. For a review of this technique, see Verma et al. (Human Chromosomes: A Manual of Basic Techniques (Pergamon Press, New York, 1988)).

Reagents for chromosome mapping can be used  
15 individually to mark a single chromosome or a single site on that chromosome, or panels of reagents can be used for marking multiple sites and/or multiple chromosomes. Reagents corresponding to noncoding regions of the genes actually are preferred for mapping purposes. Coding  
20 sequences are more likely to be conserved within gene families, thus increasing the chance of cross hybridizations during chromosomal mapping.

Once a sequence has been mapped to a precise chromosomal location, the physical position of the  
25 sequence on the chromosome can be correlated with genetic map data. (Such data are found, for example, in V. McKusick, Mendelian Inheritance in Man, available on-line through Johns Hopkins University Welch Medical Library). The relationship between genes and disease, mapped to the  
30 same chromosomal region, can then be identified through linkage analysis (co-inheritance of physically adjacent genes), described in, e.g., Egeland et al. (1987) *Nature* 325:783-787.

Moreover, differences in the DNA sequences between  
35 individuals affected and unaffected with a disease

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associated with the Tango-77 gene can be determined. If a mutation is observed in some or all of the affected individuals but not in any unaffected individuals, then the mutation is likely to be the causative agent of the particular disease. Comparison of affected and unaffected individuals generally involves first looking for structural alterations in the chromosomes such as deletions or translocations that are visible from chromosome spreads or detectable using PCR based on that DNA sequence. Ultimately, complete sequencing of genes from several individuals can be performed to confirm the presence of a mutation and to distinguish mutations from polymorphisms.

## 2. Tissue Typing

The Tango-77 sequences of the present invention can also be used to identify individuals from minute biological samples. The United States military, for example, is considering the use of restriction fragment length polymorphism (RFLP) for identification of its personnel. In this technique, an individual's genomic DNA is digested with one or more restriction enzymes, and probed on a Southern blot to yield unique bands for identification. This method does not suffer from the current limitations of "Dog Tags" which can be lost, switched, or stolen, making positive identification difficult. The sequences of the present invention are useful as additional DNA markers for RFLP (described in U.S. Patent 5,272,057).

Furthermore, the sequences of the present invention can be used to provide an alternative technique which determines the actual base-by-base DNA sequence of selected portions of an individual's genome. Thus, the Tango-77 sequences described herein can be used to prepare two PCR primers from the 5' and 3' ends of the

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sequences. These primers can then be used to amplify an individual's DNA and subsequently sequence it.

Panels of corresponding DNA sequences from individuals, prepared in this manner, can provide unique individual identifications, as each individual will have a unique set of such DNA sequences due to allelic differences. The sequences of the present invention can be used to obtain such identification sequences from individuals and from tissue. The Tango-77 sequences of the invention uniquely represent portions of the human genome. Allelic variation occurs to some degree in the coding regions of these sequences, and to a greater degree in the noncoding regions. It is estimated that allelic variation between individual humans occurs with a frequency of about once per each 500 bases. Each of the sequences described herein can, to some degree, be used as a standard against which DNA from an individual can be compared for identification purposes. Because greater numbers of polymorphisms occur in the noncoding regions, fewer sequences are necessary to differentiate individuals. The noncoding sequences of SEQ ID NO:1 can comfortably provide positive individual identification with a panel of perhaps 10 to 1,000 primers which each yield a noncoding amplified sequence of 100 bases. If predicted coding sequences, such as those in SEQ ID NO:3, SEQ ID NO:6, or SEQ ID NO:10 are used, a more appropriate number of primers for positive individual identification would be 500-2,000.

If a panel of reagents from Tango-77 sequences described herein is used to generate a unique identification database for an individual, those same reagents can later be used to identify tissue from that individual. Using the unique identification database, positive identification of the individual, living or dead, can be made from extremely small tissue samples.

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### 3. Use of Partial Tango-77 Sequences in Forensic

#### Biology

DNA-based identification techniques can also be used in forensic biology. Forensic biology is a scientific field employing genetic typing of biological evidence found at a crime scene as a means for positively identifying, for example, a perpetrator of a crime. To make such an identification, PCR technology can be used to amplify DNA sequences taken from very small biological samples such as tissues, e.g., hair or skin, or body fluids, e.g., blood, saliva, or semen found at a crime scene. The amplified sequence can then be compared to a standard, thereby allowing identification of the origin of the biological sample.

The sequences of the present invention can be used to provide polynucleotide reagents, e.g., PCR primers, targeted to specific loci in the human genome, which can enhance the reliability of DNA-based forensic identifications by, for example, providing another "identification marker" (i.e. another DNA sequence that is unique to a particular individual). As mentioned above, actual base sequence information can be used for identification as an accurate alternative to patterns formed by restriction enzyme generated fragments. Sequences targeted to noncoding regions of SEQ ID NO:1 are particularly appropriate for this use as greater numbers of polymorphisms occur in the noncoding regions, making it easier to differentiate individuals using this technique. Examples of polynucleotide reagents include the Tango-77 sequences or portions thereof, e.g., fragments derived from the noncoding regions of SEQ ID NO:1 having a length of at least 20 or 30 bases.

The Tango-77 sequences described herein can further be used to provide polynucleotide reagents, e.g., labeled or labelable probes which can be used in, for

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example, an in situ hybridization technique, to identify a specific tissue, e.g., brain tissue. This can be very useful in cases where a forensic pathologist is presented with a tissue of unknown origin. Panels of such Tango-77 probes can be used to identify tissue by species and/or by organ type.

In a similar fashion, these reagents, e.g., Tango-77 primers or probes can be used to screen tissue culture for contamination (i.e., screen for the presence of a mixture of different types of cells in a culture).

### C. Predictive Medicine

The present invention also pertains to the field of predictive medicine in which diagnostic assays, prognostic assays, pharmacogenomics, and monitoring clinical trails are used for prognostic (predictive) purposes to thereby treat an individual prophylactically. Accordingly, one aspect of the present invention relates to diagnostic assays for determining Tango-77 protein and/or nucleic acid expression as well as Tango-77 activity, in the context of a biological sample (e.g., blood, serum, cells, tissue) to thereby determine whether an individual is afflicted with a disease or disorder, or is at risk of developing a disorder, associated with aberrant Tango-77 expression or activity. The invention also provides for prognostic (or predictive) assays for determining whether an individual is at risk of developing a disorder associated with Tango-77 protein, nucleic acid expression or activity. For example, mutations in a Tango-77 gene can be assayed in a biological sample. Such assays can be used for prognostic or predictive purpose to thereby prophylactically treat an individual prior to the onset of a disorder characterized by or associated with Tango-77 protein, nucleic acid expression or activity.



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Another aspect of the invention provides methods for determining Tango-77 protein, nucleic acid expression or Tango-77 activity in an individual to thereby select appropriate therapeutic or prophylactic agents for that individual (referred to herein as "pharmacogenomics"). Pharmacogenomics allows for the selection of agents (e.g., drugs) for therapeutic or prophylactic treatment of an individual based on the genotype of the individual (e.g., the genotype of the individual examined to determine the ability of the individual to respond to a particular agent.)

Yet another aspect of the invention pertains to monitoring the influence of agents (e.g., drugs or other compounds) on the expression or activity of Tango-77 in clinical trials.

These and other agents are described in further detail in the following sections.

#### 1. Diagnostic Assays

An exemplary method for detecting the presence or absence of Tango-77 in a biological sample involves obtaining a biological sample from a test subject and contacting the biological sample with a compound or an agent capable of detecting Tango-77 protein or nucleic acid (e.g., mRNA, genomic DNA) that encodes Tango-77 protein such that the presence of Tango-77 is detected in the biological sample. A preferred agent for detecting Tango-77 mRNA or genomic DNA is a labeled nucleic acid probe capable of hybridizing to Tango-77 mRNA or genomic DNA. The nucleic acid probe can be, for example, a full-length Tango-77 nucleic acid, such as the nucleic acid of SEQ ID NO: 1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or a portion thereof, such as an oligonucleotide of at least 15, 30, 50, 100, 250 or 500 nucleotides in length and sufficient to specifically hybridize under stringent

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conditions to Tango-77 mRNA or genomic DNA. Other suitable probes for use in the diagnostic assays of the invention are described herein.

A preferred agent for detecting Tango-77 protein is an antibody capable of binding to Tango-77 protein, preferably an antibody with a detectable label. Antibodies can be polyclonal, or more preferably, monoclonal. An intact antibody, or a fragment thereof (e.g., Fab or F(ab')<sub>2</sub>) can be used. The term "labeled", with regard to the probe or antibody, is intended to encompass direct labeling of the probe or antibody by coupling (i.e., physically linking) a detectable substance to the probe or antibody, as well as indirect labeling of the probe or antibody by reactivity with another reagent that is directly labeled. Examples of indirect labeling include detection of a primary antibody using a fluorescently labeled secondary antibody and end-labeling of a DNA probe with biotin such that it can be detected with fluorescently labeled streptavidin. The term "biological sample" is intended to include tissues, cells and biological fluids isolated from a subject, as well as tissues, cells and fluids present within a subject. That is, the detection method of the invention can be used to detect Tango-77 mRNA, protein, or genomic DNA in a biological sample *in vitro* as well as *in vivo*. For example, *in vitro* techniques for detection of Tango-77 mRNA include Northern hybridizations and *in situ* hybridizations. *In vitro* techniques for detection of Tango-77 protein include enzyme linked immunosorbent assays (ELISAs), Western blots, immunoprecipitations and immunofluorescence. *In vitro* techniques for detection of Tango-77 genomic DNA include Southern hybridizations. Furthermore, *in vivo* techniques for detection of Tango-77 protein include introducing into a subject a labeled anti-Tango-77 antibody. For example, the antibody can be

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labeled with a radioactive marker whose presence and location in a subject can be detected by standard imaging techniques.

In one embodiment, the biological sample contains protein molecules from the test subject. Alternatively, the biological sample can contain mRNA molecules from the test subject or genomic DNA molecules from the test subject. A preferred biological sample is a peripheral blood leukocyte sample isolated by conventional means from a subject.

In another embodiment, the methods further involve obtaining a control biological sample from a control subject, contacting the control sample with a compound or agent capable of detecting Tango-77 protein, mRNA, or genomic DNA, such that the presence of Tango-77 protein, mRNA or genomic DNA is detected in the biological sample, and comparing the presence of Tango-77 protein, mRNA or genomic DNA in the control sample with the presence of Tango-77 protein, mRNA or genomic DNA in the test sample.

The invention also encompasses kits for detecting the presence of Tango-77 in a biological sample (a test sample). Such kits can be used to determine if a subject is suffering from or is at increased risk of developing a disorder associated with aberrant expression of Tango-77 (e.g., an immunological disorder). For example, the kit can comprise a labeled compound or agent capable of detecting Tango-77 protein or mRNA in a biological sample and means for determining the amount of Tango-77 in the sample (e.g., an anti-Tango-77 antibody or an oligonucleotide probe which binds to DNA encoding Tango-77, e.g., SEQ ID NO:1 or SEQ ID NO:3 or SEQ ID NO:6, or SEQ ID NO:10). Kits may also include instruction for observing that the tested subject is suffering from or is at risk of developing a disorder associated with aberrant expression of Tango-77 if the

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amount of Tango-77 protein or mRNA is above or below a normal level.

For antibody-based kits, the kit may comprise, for example: (1) a first antibody (e.g., attached to a solid support) which binds to Tango-77 protein; and, optionally (2) a second, different antibody which binds to Tango-77 protein or the first antibody and is conjugated to a detectable agent.

For oligonucleotide-based kits, the kit may comprise, for example: (1) an oligonucleotide, e.g., a detectably labelled oligonucleotide, which hybridizes to a Tango-77 nucleic acid sequence or (2) a pair of primers useful for amplifying a Tango-77 nucleic acid molecule;

The kit may also comprise, e.g., a buffering agent, a preservative, or a protein stabilizing agent. The kit may also comprise components necessary for detecting the detectable agent (e.g., an enzyme or a substrate). The kit may also contain a control sample or a series of control samples which can be assayed and compared to the test sample contained. Each component of the kit is usually enclosed within an individual container and all of the various containers are within a single package along with instructions for observing whether the tested subject is suffering from or is at risk of developing a disorder associated with aberrant expression of Tango-77.

## 2. Prognostic Assays

The methods described herein can furthermore be utilized as diagnostic or prognostic assays to identify subjects having or at risk of developing a disease or disorder associated with aberrant Tango-77 expression or activity. For example, the assays described herein, such as the preceding diagnostic assays or the following assays, can be utilized to identify a subject having or

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at risk of developing a disorder associated with aberrant expression or activity. Thus, the present invention provides a method in which a test sample is obtained from a subject and Tango-77 protein or nucleic acid (e.g., mRNA, genomic DNA) is detected, wherein the presence of Tango-77 protein or nucleic acid is diagnostic for a subject having or at risk of developing a disease or disorder associated with aberrant Tango-77 expression or activity. As used herein, a "test sample" refers to a biological sample obtained from a subject of interest. For example, a test sample can be a biological fluid (e.g., serum), cell sample, or tissue.

Furthermore, the prognostic assays described herein can be used to determine whether a subject can be administered an agent (e.g., an agonist, antagonist, peptidomimetic, protein, peptide, nucleic acid, small molecule, or other drug candidate) to treat a disease or disorder associated with aberrant Tango-77 expression or activity. For example, such methods can be used to determine whether a subject can be effectively treated with a specific agent or class of agents (e.g., agents of a type which decrease Tango-77 activity). Thus, the present invention provides methods for determining whether a subject can be effectively treated with an agent for a disorder associated with aberrant Tango-77 expression or activity in which a test sample is obtained and Tango-77 protein or nucleic acid is detected (e.g., wherein the presence of Tango-77 protein or nucleic acid is diagnostic for a subject that can be administered the agent to treat a disorder associated with aberrant Tango-77 expression or activity).

The methods of the invention can also be used to detect genetic lesions or mutations in a Tango-77 gene, thereby determining if a subject with the lesioned gene is at risk for a disorder characterized by aberrant

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inflammation. In preferred embodiments, the methods include detecting, in a sample of cells from the subject, the presence or absence of a genetic lesion or mutation characterized by at least one of an alteration affecting  
5 the integrity of a gene encoding a Tango-77-protein, or the mis-expression of the Tango-77 gene. For example, such genetic lesions or mutations can be detected by ascertaining the existence of at least one of: 1) a deletion of one or more nucleotides from a Tango-77 gene;  
10 2) an addition of one or more nucleotides to a Tango-77 gene; 3) a substitution of one or more nucleotides of a Tango-77 gene; 4) a chromosomal rearrangement of a Tango-77 gene; 5) an alteration in the level of a messenger RNA transcript of a Tango-77 gene; 6) an  
15 aberrant modification of a Tango-77 gene, such as of the methylation pattern of the genomic DNA; 7) the presence of a non-wild type splicing pattern of a messenger RNA transcript of a Tango-77 gene; 8) a non-wild type level of a Tango-77-protein; 9) an allelic loss of a Tango-77  
20 gene, and 10) an inappropriate post-translational modification of a Tango-77-protein. As described herein, there are a large number of assay techniques known in the art which can be used for detecting lesions or mutations in a Tango-77 gene. A preferred biological sample is a  
25 peripheral blood leukocyte sample isolated by conventional means from a subject.

In certain embodiments, detection of the lesion involves the use of a probe/primer in a polymerase chain reaction (PCR) (*see, e.g.,* U.S. Patent Nos. 4,683,195 and  
30 4,683,202), such as anchor PCR or RACE PCR, or, alternatively, in a ligation chain reaction (LCR) (*see, e.g.,* Landegran et al. (1988) *Science* 241:1077-1080; and Nakazawa et al. (1994) *Proc. Natl. Acad. Sci. USA* 91:360-364), the latter of which can be particularly useful for  
35 detecting point mutations in the Tango-77-gene (*see,*

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e.g., Abravaya et al. (1995) *Nucleic Acids Res.* 23:675-682). This method can include the steps of collecting a sample of cells from a patient, isolating nucleic acid (e.g., genomic, mRNA or both) from the cells of the sample, contacting the nucleic acid sample with one or more primers which specifically hybridize to a Tango-77 gene under conditions such that hybridization and amplification of the Tango-77-gene (if present) occurs, and detecting the presence or absence of an amplification product, or detecting the size of the amplification product and comparing the length to a control sample. It is anticipated that PCR and/or LCR may be desirable to use as a preliminary amplification step in conjunction with any of the techniques used for detecting mutations described herein.

Alternative amplification methods include: self sustained sequence replication (Guatelli et al. (1990) *Proc. Natl. Acad. Sci. USA* 87:1874-1878), transcriptional amplification system (Kwoh, et al. (1989) *Proc. Natl. Acad. Sci. USA* 86:1173-1177), Q-Beta Replicase (Lizardi et al. (1988) *Bio/Technology* 6:1197), or any other nucleic acid amplification method, followed by the detection of the amplified molecules using techniques well known to those of skill in the art. These detection schemes are especially useful for the detection of nucleic acid molecules if such molecules are present in very low numbers.

In an alternative embodiment, mutations in a Tango-77 gene from a sample cell can be identified by alterations in restriction enzyme cleavage patterns. For example, sample and control DNA is isolated, amplified (optionally), digested with one or more restriction endonucleases, and fragment length sizes are determined by gel electrophoresis and compared. Differences in fragment length sizes between sample and control DNA

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indicates mutations in the sample DNA. Moreover, the use of sequence specific ribozymes (see, e.g., U.S. Patent No. 5,498,531) can be used to score for the presence of specific mutations by development or loss of a ribozyme cleavage site.

In other embodiments, genetic mutations in Tango-77 can be identified by hybridizing a sample and control nucleic acids, e.g., DNA or RNA, to high density arrays containing hundreds or thousands of oligonucleotides probes (Cronin et al. (1996) *Human Mutation* 7:244-255; Kozal et al. (1996) *Nature Medicine* 2:753-759). For example, genetic mutations in Tango-77 can be identified in two-dimensional arrays containing light-generated DNA probes as described in Cronin et al. supra. Briefly, a first hybridization array of probes can be used to scan through long stretches of DNA in a sample and control to identify base changes between the sequences by making linear arrays of sequential overlapping probes. This step allows the identification of point mutations. This step is followed by a second hybridization array that allows the characterization of specific mutations by using smaller, specialized probe arrays complementary to all variants or mutations detected. Each mutation array is composed of parallel probe sets, one complementary to the wild-type gene and the other complementary to the mutant gene.

In yet another embodiment, any of a variety of sequencing reactions known in the art can be used to directly sequence the Tango-77 gene and detect mutations by comparing the sequence of the sample Tango-77 with the corresponding wild-type (control) sequence. Examples of sequencing reactions include those based on techniques developed by Maxim and Gilbert ((1977) *Proc. Natl. Acad. Sci. USA* 74:560) or Sanger ((1977) *Proc. Natl. Acad. Sci. USA* 74:5463). It is also contemplated that any of a



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variety of automated sequencing procedures can be utilized when performing the diagnostic assays ((1995) *Bio/Techniques* 19:448), including sequencing by mass spectrometry (see, e.g., PCT Publication No. WO 94/16101; 5 Cohen et al. (1996) *Adv. Chromatogr.* 36:127-162; and Griffin et al. (1993) *Appl. Biochem. Biotechnol.* 38:147-159).

Other methods for detecting mutations in the Tango-77 gene include methods in which protection from 10 cleavage agents is used to detect mismatched bases in RNA/RNA or RNA/DNA heteroduplexes (Myers et al. (1985) *Science* 230:1242). In general, the technique of "mismatch cleavage" entails providing heteroduplexes formed by hybridizing (labeled) RNA or DNA containing the 15 wild-type Tango-77 sequence with potentially mutant RNA or DNA obtained from a tissue sample. The double-stranded duplexes are treated with an agent which cleaves single-stranded regions of the duplex such as which will exist due to basepair mismatches between the control and 20 sample strands. RNA/DNA duplexes can be treated with RNase to digest mismatched regions, and DNA/DNA hybrids can be treated with S1 nuclease to digest mismatched regions. In other embodiments, either DNA/DNA or RNA/DNA duplexes can be treated with hydroxylamine or osmium 25 tetroxide and with piperidine in order to digest mismatched regions. After digestion of the mismatched regions, the resulting material is then separated by size on denaturing polyacrylamide gels to determine the site of mutation. See, e.g., Cotton et al. (1988) *Proc. Natl. Acad. Sci. USA* 85:4397; Saleeba et al. (1992) *Methods Enzymol.* 217:286-295. In a preferred embodiment, the 30 control DNA or RNA can be labeled for detection.

In still another embodiment, the mismatch cleavage reaction employs one or more proteins that recognize 35 mismatched base pairs in double-stranded DNA (so called

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"DNA mismatch repair" enzymes) in defined systems for detecting and mapping point mutations in Tango-77 cDNAs obtained from samples of cells. For example, the mutY enzyme of *E. coli* cleaves A at G/A mismatches and the thymidine DNA glycosylase from HeLa cells cleaves T at G/T mismatches (Hsu et al. (1994) *Carcinogenesis* 15:1657-1662). According to an exemplary embodiment, a probe based on a Tango-77 sequence, e.g., a wild-type Tango-77 sequence, is hybridized to a cDNA or other DNA product from a test cell(s). The duplex is treated with a DNA mismatch repair enzyme, and the cleavage products, if any, can be detected from electrophoresis protocols or the like. See, e.g., U.S. Patent No. 5,459,039.

In other embodiments, alterations in electrophoretic mobility will be used to identify mutations in Tango-77 genes. For example, single strand conformation polymorphism (SSCP) may be used to detect differences in electrophoretic mobility between mutant and wild type nucleic acids (Orita et al. (1989) *Proc. Natl. Acad. Sci. USA* 86:2766; see also Cotton (1993) *Mutat. Res.* 285:125-144; Hayashi (1992) *Genet Anal Tech Appl* 9:73-79). Single-stranded DNA fragments of sample and control Tango-77 nucleic acids will be denatured and allowed to renature. The secondary structure of single-stranded nucleic acids varies according to sequence, and the resulting alteration in electrophoretic mobility enables the detection of even a single base change. The DNA fragments may be labeled or detected with labeled probes. The sensitivity of the assay may be enhanced by using RNA (rather than DNA), in which the secondary structure is more sensitive to a change in sequence. In a preferred embodiment, the subject method utilizes heteroduplex analysis to separate double stranded heteroduplex molecules on the basis of changes in

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electrophoretic mobility (Keen et al. (1991) *Trends Genet* 7:5).

In yet another embodiment, the movement of mutant or wild-type fragments in polyacrylamide gels containing  
5 a gradient of denaturant is assayed using denaturing gradient gel electrophoresis (DGGE) (Myers et al. (1985) *Nature* 313:495). When DGGE is used as the method of analysis, DNA will be modified to insure that it does not completely denature, for example by adding a GC clamp of  
10 approximately 40 bp of high-melting GC-rich DNA by PCR. In a further embodiment, a temperature gradient is used in place of a denaturing gradient to identify differences in the mobility of control and sample DNA (Rosenbaum and Reissner (1987) *Biophys. Chem.* 265:12753).

15 Examples of other techniques for detecting point mutations include, but are not limited to, selective oligonucleotide hybridization, selective amplification, or selective primer extension. For example, oligonucleotide primers may be prepared in which the  
20 known mutation is placed centrally and then hybridized to target DNA under conditions which permit hybridization only if a perfect match is found (Saiki et al. (1986) *Nature* 324:163); Saiki et al. (1989) *Proc. Natl. Acad. Sci. USA* 86:6230). Such allele specific oligonucleotides  
25 are hybridized to PCR amplified target DNA or a number of different mutations when the oligonucleotides are attached to the hybridizing membrane and hybridized with labeled target DNA.

Alternatively, allele specific amplification  
30 technology which depends on selective PCR amplification may be used in conjunction with the instant invention. Oligonucleotides used as primers for specific amplification may carry the mutation of interest in the center of the molecule (so that amplification depends on  
35 differential hybridization) (Gibbs et al. (1989) *Nucleic*

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Acids Res. 17:2437-2448) or at the extreme 3' end of one primer where, under appropriate conditions, mismatch can prevent or reduce polymerase extension (Prossner (1993) Tibtech 11:238). In addition, it may be desirable to  
5 introduce a novel restriction site in the region of the mutation to create cleavage-based detection (Gasparini et al. (1992) Mol. Cell Probes 6:1). It is anticipated that in certain embodiments amplification may also be performed using Taq ligase for amplification (Barany  
10 (1991) Proc. Natl. Acad. Sci USA 88:189). In such cases, ligation will occur only if there is a perfect match at the 3' end of the 5' sequence making it possible to detect the presence of a known mutation at a specific site by looking for the presence or absence of  
15 amplification.

The methods described herein may be performed, for example, by utilizing pre-packaged diagnostic kits comprising at least one probe nucleic acid or antibody reagent described herein, which may be conveniently used,  
20 e.g., in clinical settings to diagnose patients exhibiting symptoms or family history of a disease or illness involving a Tango-77 gene.

Furthermore, any cell type or tissue, preferably peripheral blood leukocytes, in which Tango-77 is  
25 expressed may be utilized in the prognostic assays described herein.

### 3. Pharmacogenomics

Agents, or modulators which have a stimulatory or  
30 inhibitory effect on Tango-77 activity (e.g., Tango-77 gene expression) as identified by a screening assay described herein can be administered to individuals to treat (prophylactically or therapeutically) disorders (e.g., acute or chronic inflammation and asthma)  
35 associated with aberrant Tango-77 activity. In

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conjunction with such treatment, the pharmacogenomics (i.e., the study of the relationship between an individual's genotype and that individual's response to a foreign compound or drug) of the individual may be considered. Differences in metabolism of therapeutics can lead to severe toxicity or therapeutic failure by altering the relation between dose and blood concentration of the pharmacologically active drug. Thus, the pharmacogenomics of the individual permits the selection of effective agents (e.g., drugs) for prophylactic or therapeutic treatments based on a consideration of the individual's genotype. Such pharmacogenomics can further be used to determine appropriate dosages and therapeutic regimens.

Accordingly, the activity of Tango-77 protein, expression of Tango-77 nucleic acid, or mutation content of Tango-77 genes in an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual.

Pharmacogenomics deals with clinically significant hereditary variations in the response to drugs due to altered drug disposition and abnormal action in affected persons. See, e.g., Linder (1997) *Clin. Chem.* 43(2):254-266. In general, two types of pharmacogenetic conditions can be differentiated. Genetic conditions transmitted as a single factor altering the way drugs act on the body are referred to as "altered drug action." Genetic conditions transmitted as single factors altering the way the body acts on drugs are referred to as "altered drug metabolism". These pharmacogenetic conditions can occur either as rare defects or as polymorphisms. For example, glucose-6-phosphate dehydrogenase deficiency (G6PD) is a common inherited enzymopathy in which the main clinical complication is haemolysis after ingestion of oxidant drugs (anti-

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malarials, sulfonamides, analgesics, nitrofurans) and consumption of fava beans.

As an illustrative embodiment, the activity of drug metabolizing enzymes is a major determinant of both the intensity and duration of drug action. The discovery of genetic polymorphisms of drug metabolizing enzymes (e.g., N-acetyltransferase 2 (NAT 2) and cytochrome P450 enzymes CYP2D6 and CYP2C19) has provided an explanation as to why some patients do not obtain the expected drug effects or show exaggerated drug response and serious toxicity after taking the standard and safe dose of a drug. These polymorphisms are expressed in two phenotypes in the population, the extensive metabolizer (EM) and poor metabolizer (PM). The prevalence of PM is different among different populations. For example, the gene coding for CYP2D6 is highly polymorphic and several mutations have been identified in PM, which all lead to the absence of functional CYP2D6. Poor metabolizers of CYP2D6 and CYP2C19 quite frequently experience exaggerated drug response and side effects when they receive standard doses. If a metabolite is the active therapeutic moiety, PM shows no therapeutic response, as demonstrated for the analgesic effect of codeine mediated by its CYP2D6-formed metabolite morphine. The other extreme are the so called ultra-rapid metabolizers who do not respond to standard doses. Recently, the molecular basis of ultra-rapid metabolism has been identified to be due to CYP2D6 gene amplification.

Thus, the activity of Tango-77 protein, expression of Tango-77 nucleic acid, or mutation content of Tango-77 genes in an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual. In addition, pharmacogenetic studies can be used to apply genotyping of polymorphic alleles encoding drug-metabolizing enzymes

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to the identification of an individual's drug responsiveness phenotype. This knowledge, when applied to dosing or drug selection, can avoid adverse reactions or therapeutic failure and thus enhance therapeutic or prophylactic efficiency when treating a subject with a Tango-77 modulator, such as a modulator identified by one of the exemplary screening assays described herein.

#### 4. Monitoring of Effects During Clinical Trials

Monitoring the influence of agents (e.g., drugs, compounds) on the expression or activity of Tango-77 (e.g., the ability to modulate aberrant inflammation) can be applied not only in basic drug screening, but also in clinical trials. For example, the effectiveness of an agent, as determined by a screening assay as described herein, to increase Tango-77 gene expression, increase protein levels, or upregulate Tango-77 activity, can be monitored in clinical trials of subjects exhibiting decreased Tango-77 gene expression, decreased protein levels, or downregulated Tango-77 activity. Alternatively, the effectiveness of an agent, as determined by a screening assay, to decrease Tango-77 gene expression, decrease protein levels, or downregulate Tango-77 activity, can be monitored in clinical trials of subjects exhibiting increased Tango-77 gene expression, increased protein levels, or upregulated Tango-77 activity.

For example, and not by way of limitation, genes, including Tango-77, that are modulated in cells by treatment with an agent (e.g., compound, drug or small molecule) which modulates Tango-77 activity (e.g., as identified in a screening assay described herein) can be identified. Thus, to study the effect of agents on cellular proliferation disorders, for example, in a clinical trial, cells can be isolated and RNA prepared

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and analyzed for the levels of expression of Tango-77 and other genes implicated in the disorder. The levels of gene expression (i.e., a gene expression pattern) can be quantified by Northern blot analysis or RT-PCR, as described herein, or alternatively by measuring the amount of protein produced, by one of the methods as described herein, or by measuring the levels of activity of Tango-77 or other genes. In this way, the gene expression pattern can serve as a marker, indicative of the physiological response of the cells to the agent. Accordingly, this response state may be determined before, and at various points during, treatment of the individual with the agent.

In a preferred embodiment, the present invention provides a method for monitoring the effectiveness of treatment of a subject with an agent (e.g., an agonist, antagonist, peptidomimetic, protein, peptide, nucleic acid, small molecule, or other drug candidate identified by the screening assays described herein) comprising the steps of (i) obtaining a pre-administration sample from a subject prior to administration of the agent; (ii) detecting the level of expression of a Tango-77 protein, mRNA, or genomic DNA in the preadministration sample; (iii) obtaining one or more post-administration samples from the subject; (iv) detecting the level of expression or activity of the Tango-77 protein, mRNA, or genomic DNA in the post-administration samples; (v) comparing the level of expression or activity of the Tango-77 protein, mRNA, or genomic DNA in the pre-administration sample with the Tango-77 protein, mRNA, or genomic DNA in the post administration sample or samples; and (vi) altering the administration of the agent to the subject accordingly. For example, increased administration of the agent may be desirable to increase the expression or activity of Tango-77 to higher levels than detected,



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i.e., to increase the effectiveness of the agent.  
Alternatively, decreased administration of the agent may  
be desirable to decrease expression or activity of  
Tango-77 to lower levels than detected, i.e., to decrease  
5 the effectiveness of the agent.

### C. Methods of Treatment

The present invention provides for both  
prophylactic and therapeutic methods of treating a  
subject at risk of (or susceptible to) developing or  
10 having a disorder associated with aberrant Tango-77  
expression or activity. Alternatively, disorders  
associated with aberrant IL-1 production can be treated  
with Tango-77. Such disorders include acute and chronic  
inflammation, asthma, some classes of arthritis,  
15 autoimmune diabetes, systemic lupus erythematosus and  
inflammatory bowel disease.

#### 1. Prophylactic Methods

In one aspect, the invention provides a method for  
preventing in a subject, a disease or condition  
20 associated with an aberrant Tango-77 expression or  
activity (or aberrant IL-1 expression or activity), by  
administering to the subject an agent which modulates  
Tango-77 expression or at least one Tango-77 activity.  
Subjects at risk for a disease which is caused or  
25 contributed to by aberrant Tango-77 expression or  
activity can be identified by, for example, any or a  
combination of diagnostic or prognostic assays as  
described herein. Administration of a prophylactic agent  
can occur prior to the manifestation of symptoms  
30 characteristic of the Tango-77 aberrancy, such that a  
disease or disorder is prevented or, alternatively,  
delayed in its progression. Depending on the type of  
Tango-77 aberrancy, for example, a Tango-77 agonist or  
Tango-77 antagonist agent can be used for treating the

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subject. The appropriate agent can be determined based on screening assays described herein.

## 2. Therapeutic Methods

Another aspect of the invention pertains to  
5 methods of modulating Tango-77 expression or activity for  
therapeutic purposes. The modulatory method of the  
invention involves contacting a cell with an agent that  
modulates one or more of the activities of Tango-77  
protein activity associated with the cell. An agent that  
10 modulates Tango-77 protein activity can be an agent as  
described herein, such as a nucleic acid or a protein, a  
naturally-occurring cognate ligand of a Tango-77 protein,  
a peptide, a Tango-77 peptidomimetic, or other small  
molecule. In one embodiment, the agent stimulates one or  
15 more of the biological activities of Tango-77 protein.  
Examples of such stimulatory agents include active  
Tango-77 protein and a nucleic acid molecule encoding  
Tango-77 that has been introduced into the cell. In  
another embodiment, the agent inhibits one or more of the  
20 biological activities of Tango-77 protein. Examples of  
such inhibitory agents include antisense Tango-77 nucleic  
acid molecules and anti-Tango-77 antibodies. These  
modulatory methods can be performed in vitro (e.g., by  
culturing the cell with the agent) or, alternatively, in  
25 vivo (e.g., by administering the agent to a subject). As  
such, the present invention provides methods of treating  
an individual afflicted with a disease or disorder  
characterized by aberrant expression or activity of a  
Tango-77 protein or nucleic acid molecule. In one  
30 embodiment, the method involves administering an agent  
(e.g., an agent identified by a screening assay described  
herein), or combination of agents that modulates (e.g.,  
upregulates or downregulates) Tango-77 expression or  
activity. In another embodiment, the method involves

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administering a Tango-77 protein or nucleic acid molecule as therapy to compensate for reduced or aberrant Tango-77 expression or activity.

Stimulation of Tango-77 activity is desirable in situations in which Tango-77 is abnormally downregulated and/or in which increased Tango-77 activity is likely to have a beneficial effect. Conversely, inhibition of Tango-77 activity is desirable in situations in which Tango-77 is abnormally upregulated and/or in which decreased Tango-77 activity is likely to have a beneficial effect.

This invention is further illustrated by the following examples which should not be construed as limiting. The contents of all references, patents and published patent applications cited throughout this application are hereby incorporated by reference.

#### EXAMPLES

##### Example 1: Isolation and Characterization of Human Tango-77 cDNAs

Cytokine genes IL-1 $\alpha$ , IL-1 $\beta$  and IL-1ra have been found to be closely clustered on chromosome 2, i.e., IL-1 $\alpha$ , IL-1 $\beta$  and IL-1ra are located within 450 kb of each other. BAC clones containing IL-1 $\alpha$  and IL-1 $\beta$  were used to identify other proximal unknown cytokine genes. To do this, a BAC clone containing IL-1 $\alpha$  and IL-1 $\beta$  was selected from a BAC library (Research Genetics, Huntsville, Alabama) using specific primers designed against IL-1 $\alpha$  and IL-1 $\beta$ . The DNA from the BAC was extracted and used to make a random-sheared genomic library. From this BAC library, 4000 clones were selected for sequencing. The resulting genomic sequences were then assembled into contigs and used to screen proprietary and public data bases. One genomic contig was found to contain two

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segments of sequences which resemble IL-1ra. These two segments are potential exons of Tango-77 gene.

Two PCR primers were then designed from the two potential exons and used to screen a panel of cDNA  
5 libraries for the expression of a Tango-77 message. A cDNA library from TNF- $\alpha$  treated human lung epithelia showed a positive band of the predicted size (i.e., if the two exons are spliced together). Using the PCR fragment as a probe, a single cDNA clone was isolated  
10 from the same library. This cDNA contains an insert of 989 bp. The cDNA clone contains three possible open reading frames. The first open reading frame encompasses 534 nucleotides (nucleotides 356-889 of SEQ ID NO:1; SEQ ID NO:3) and encodes a 178 amino acid protein (SEQ ID  
15 NO:2). This protein may include a predicted signal sequence of about 63 amino acids (from amino acid 1 to about amino acid 63 of SEQ ID NO:2 (SEQ ID NO:4)) and a predicted mature protein of about 115 amino acids (from about amino acid 64 to amino acid 178 of SEQ ID NO:2 (SEQ  
20 ID NO:5)).

The second putative nucleotide open reading frame encompasses 498 nucleotides (nucleotides 389-889 of SEQ ID NO:1; SEQ ID NO:6) and encodes a 167 amino acid protein (SEQ ID NO:7). This protein includes a predicted  
25 signal sequence of about 52 amino acids (from amino acid 1 to about amino acid 52 of SEQ ID NO:7 (SEQ ID NO:8)) and a predicted mature protein of about 115 amino acids (from about amino acid 53 to amino acid 167 of SEQ ID NO:7 (SEQ ID NO:9)).

30 The third open reading frame (nucleotides 372-889 of SEQ ID NO:1; SEQ ID NO:10) encompasses 408 nucleotides and encodes a 136 amino acid protein (SEQ ID NO:11). This protein includes a predicted signal sequence of about 21 amino acids (from amino acid 1 to about amino  
35 acid 21 of SEQ ID NO:11 (SEQ ID NO:12)) and a predicted

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mature protein of about 115 amino acids (from about amino acid 22 to amino acid 136 of SEQ ID NO:11 (SEQ ID NO:13)).

Tango-77 is predicted to be 35% identical to human IL-1ra at the amino acid level.

#### Example 2: Expression of Tango-77 mRNA in Human Tissues

The expression of Tango-77 was analyzed using Northern blot hybridization. A PCR generated 989 bp Tango-77 product was radioactively labeled with <sup>32</sup>P-dCTP using the Prime-It kit (Stratagene; La Jolla, CA) according to the instructions of the supplier. Filters containing human mRNA (MTNI and MTNII: Clontech; Palo Alto, CA) were probed in ExpressHyb hybridization solution (Clontech) and washed at high stringency according to manufacturer's recommendations.

Tango-77 mRNA was not detected in any unstimulated tissues (brain, liver, spleen, skeletal muscle, testis, pancreas, heart, kidney and peripheral blood leukocytes) mRNA on Clontech Northern blots.

Over 96 cDNA libraries were then tested for the presence of Tango-77 using PCR amplification. Only three libraries displayed a positive signal. These libraries were the TNF $\alpha$ -treated bronchoepithelium, TNF $\alpha$ -treated SSC cell line and anti-CD3-treated T cells.

#### Example 3: Characterization of Tango-77 Proteins

In this example, the predicted amino acid sequence of human Tango-77 protein was compared to the amino acid sequence of known protein IL-1ra. In addition, the molecular weight of the human Tango-77 proteins was predicted.

The human Tango-77 cDNA (Figure 1; SEQ ID NO:1) isolated as described above encodes a 178 amino acid protein (Figure 1; SEQ ID NO:2) or a 167 amino acid

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protein (Figure 1; SEQ ID NO:7) or a 136 amino acid protein (Figure 1; SEQ ID NO:11). The signal peptide prediction program SIGNALP Optimized Tool (Nielsen et al. (1997) *Protein Engineering* 10:1-6) predicted that

5 Tango-77 includes a 63 amino acid signal peptide (amino acid 1 to about amino acid 63 of SEQ ID NO:2 (SEQ ID NO:4)) preceding the 115 mature protein; or preceding the 115 mature protein (about amino acid 52 to amino acid 167 of SEQ ID NO:7 (SEQ ID NO:8)); or preceding the 115

10 mature protein (about amino acid 21 to amino acid 136 of SEQ ID NO:11;SEQ ID NO:12).

As shown in Figure 2, Tango-77 has a region of homology to IL-1ra (SEQ ID NO:14).

Mature Tango-77 has a predicted MW of about 13 kDa

15 and the predicted MW for the immature Tango-77 is 19.6 kDa, 18.5 kDa or 15.2 kDa, not including post-translational modifications.

#### Example 4: Preparation of Tango-77 Proteins

Recombinant Tango-77 can be produced in a variety

20 of expression systems. For example, the mature Tango-77 peptide can be expressed as a recombinant glutathione-S-transferase (GST) fusion protein in *E. coli* and the fusion protein can be isolated and characterized. Specifically, as described above, Tango-77 can be fused

25 to GST and this fusion protein can be expressed in *E. coli* strain PEB199. Expression of the GST-Tango-77 fusion protein in PEB199 can be induced with IPTG. The recombinant fusion protein can be purified from crude bacterial lysates of the induced PEB199 strain by

30 affinity chromatography on glutathione beads.

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Example 5: Alternatively spliced forms of IL-1ra and  
Tango-77

Computer program Procrustes (Gelfand et al., 1996, *Proc. Natl. Acad. Sci. USA*, 93:9061-9066) is an alignment  
5 algorithm that predicts the presence of alternatively  
spliced exons for a protein of interest in a stretch of  
genomic DNA. Using the IL-1ra sequence, Procrustes was  
used to search for the presence of additional sequences  
that might encode for alternatively spliced forms of IL-  
10 1ra in the two overlapping BAC genomic sequences (see  
Fig. 3 and Fig. 4). Potential sequences that encode  
variant exons for IL-1ra were identified. These  
predicted exons aligned well with the N-terminal region  
of IL-1ra, but were not present in Tango-77. The results  
15 from Procrustes predicts the existence of more spliced  
forms of IL-1ra.

Furthermore, Procrustes also predicted an  
additional sequence in BAC1 and BAC2 that encodes an  
alternatively spliced exon for Tango-77 (T77-procrustes;  
20 Fig. 5). This predicted splice variant form of Tango-77,  
T77-procrustes, was aligned with Tango-77 (Fig. 6) and  
with IL-1ra and IL-1 $\beta$  (Fig.7).

PCR primers within this sequence can be used to  
generate a product that can be used to screen a panel of  
25 cDNA libraries using standard techniques. Suitable cDNA  
libraries include libraries made from TNF $\alpha$ -treated  
bronchoepithelium, TNF $\alpha$ -treated SSC cell line and anti-  
CD3-treated T cells. The resulting cDNA clone(s) can be  
isolated from the library and sequenced to identify  
30 additional Tango-77 cDNAs.

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Equivalents

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific  
5 embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims.



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What is claimed is:

1. An isolated nucleic acid molecule selected from the group consisting of:
  - a) a nucleic acid molecule comprising a  
5 nucleotide sequence which is at least 45% identical to the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, or a complement thereof;
  - 10 b) a nucleic acid molecule comprising a fragment of at least 300 nucleotides of the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, or a complement thereof;
  - 15 c) nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the  
20 plasmid deposited with ATCC as Accession Number 98807;
  - d) a nucleic acid molecule which encodes a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID  
25 NO:12, SEQ ID NO:13, wherein the fragment comprises at least 15 contiguous amino acids of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or the polypeptide encoded by the cDNA insert of the plasmid  
30 deposited with ATCC as Accession Number 98807; and
  - e) a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9,

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SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, wherein the nucleic acid molecule hybridizes to a nucleic acid  
5 molecule comprising SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the complement thereof under stringent conditions.

2. The isolated nucleic acid molecule of claim 1, which is selected from the group consisting of:
- 10 a) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, or SEQ ID NO:10 or the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, or a complement thereof; and
- 15 b) a nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the  
20 plasmid deposited with ATCC as Accession Number 98807.

3. The nucleic acid molecule of claim 1 further comprising vector nucleic acid sequences.

4. The nucleic acid molecule of claim 1 further comprising nucleic acid sequences encoding a heterologous  
25 polypeptide.

5. A host cell containing the nucleic acid molecule of claim 1.

6. The host cell of claim 5 which is a mammalian host cell.

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7. A non-human mammalian host cell containing the nucleic acid molecule of claim 1.

8. An isolated polypeptide selected from the group consisting of:

5 a) a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, wherein the fragment comprises at least 15 contiguous amino acids of SEQ ID  
10 NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, or SEQ ID NO:13.

b) a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8,  
15 SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, wherein the polypeptide is encoded by a nucleic acid molecule which hybridizes to a nucleic acid molecule  
20 comprising SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the complement thereof under stringent conditions;

c) a polypeptide which is encoded by a nucleic acid molecule comprising a nucleotide sequence which is  
25 at least 55% identical to a nucleic acid comprising the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, or SEQ ID NO:10.

9. The isolated polypeptide of claim 8 comprising the amino acid sequence of SEQ ID NO:2, SEQ ID  
30 NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807.

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10. The polypeptide of claim 8 further comprising heterologous amino acid sequences.

11. An antibody which selectively binds to a polypeptide of claim 8.

5 12. A method for producing a polypeptide selected from the group consisting of:

a) a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID  
10 NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807;

b) a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID  
15 NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, wherein the fragment comprises at least 15 contiguous amino acids  
20 of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807; and

25 c) a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the  
30 plasmid deposited with ATCC as Accession Number 98807, wherein the polypeptide is encoded by a nucleic acid molecule which hybridizes to a nucleic acid sequence of

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SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, or SEQ ID NO:10  
under stringent conditions;

comprising culturing the host cell of claim 5  
under conditions in which the nucleic acid molecule is  
5 expressed.

13. A method for detecting the presence of a  
polypeptide of claim 8 in a sample, comprising:

- a) contacting the sample with a compound which  
selectively binds to a polypeptide of claim 8; and
- 10 b) determining whether the compound binds to the  
polypeptide in the sample.

14. The method of claim 13, wherein the compound  
which binds to the polypeptide is an antibody.

15. A kit comprising a compound which selectively  
15 binds to a polypeptide of claim 8 and instructions for  
use.

16. A method for detecting the presence of a  
nucleic acid molecule of claim 1 in a sample, comprising  
the steps of:

- 20 a) contacting the sample with a nucleic acid  
probe or primer which selectively hybridizes to the  
nucleic acid molecule; and
- b) determining whether the nucleic acid probe or  
primer binds to a nucleic acid molecule in the sample.

25 17. The method of claim 16, wherein the sample  
comprises mRNA molecules and is contacted with a nucleic  
acid probe.

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18. A kit comprising a compound which selectively hybridizes to a nucleic acid molecule of claim 1 and instructions for use.

19. A method for identifying a compound which  
5 binds to a polypeptide of claim 8 comprising the steps of:

- a) contacting a polypeptide, or a cell expressing a polypeptide of claim 8 with a test compound; and
- 10 b) determining whether the polypeptide binds to the test compound.

20. The method of claim 19, wherein the binding of the test compound to the polypeptide is detected by a method selected from the group consisting of:

- 15 a) detection of binding by direct detecting of test compound/polypeptide binding;
- b) detection of binding using a competition binding assay; and
- c) detection of binding using an assay for  
20 Tango-77-mediated signal transduction.s

21. A method for modulating the activity of a polypeptide of claim 8 comprising contacting a polypeptide or a cell expressing a polypeptide of claim 8 with a compound which binds to the polypeptide in a  
25 sufficient concentration to modulate the activity of the polypeptide.

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22. A method for identifying a compound which modulates the activity of a polypeptide of claim 8, comprising:

- a) contacting a polypeptide of claim 8 with a  
5 test compound; and
- b) determining the effect of the test compound on the activity of the polypeptide to thereby identify a compound which modulates the activity of the polypeptide.

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GTGGACCCACGGCTCCCGCAGACGTCTACCTGGGGGTCCCGTCTGCGCTCCCGGGATGGAAAACGCCCAGGGGAAACTTA 79
GGCAGGGCGAGCGGACGGGCACCTCCCGCGGGACGAACTCACTCGGTGGCCTCCTACTTCCCGGGCCGTGTTCCAACGCC 158
TGAGAATAACGGGAACAGCGGTCTGTACTCACCGACAGCGGCAGCAGCGGCCTCTCTCAATTGGGCAAAGCACTCCAGAC 237
CTTTTGGGAAGAGTGACACCAAAGGCAAGCACCTGCTTGGCAGGCCCTCAGCTTCTACGCAAGTATAAGTCTTGGACTT 316
      M S F V G E N S G V 10
CATTCCATTTTCTGTTGAGTAATAAACTCAACGTTGAAA ATG TCC TTT GTG GGG GAG AAC TCA GGA GTG 185
K M G S E D W E K D E P Q C C L E D P A 30
AAA ATG GGC TGT GAG GAC TGG GAA AAA GAT GAA CCC CAG TGC TGC TTA GAA GAC CCG GCT 445
G S P L E P G P S L P T M N F V H T K I 50
GGA AGC CCC CTG GAA CCA GGC CCA AGC CTC CCC ACC ATG AAT TTT GTT CAC ACA AAG ATC 505
F F A L A S S L S S A S A E K G S P I L 70
TTC TTT GCA TTA GCC TCA TCC TTG AGC TCA GCC TCT GCG GAG AAA GGA AGT CCG ATT CTC 565
L S V S K G E F C L Y C D K D K G Q S H 90
CTG GGG GTC TCT AAA GGG GAG TTT TGT CTC TAC TGT GAC AAG GAT AAA GGA CAA AGT CAT 625
P S L Q L K K E K L M K L A A Q K E S A 110
TCA TCC CTT CAG CTG AAG AAG GAG AAA CTG ATG AAG CTG GCT GCC CAA AAG GAA TCA GCA 685
R R P F I F Y R A Q V G S W N M L E S A 130
CGC CGG CCC TTC ATC TTT TAT AGG GCT CAG GTG GGC TCC TGG AAC ATG CTG GAG TCG GCG 745
A H P G W F I C T S C N C N E P V G V T 150
GCT CAC CCC GGA TGG TTC ATC TGC ACC TCC TGC AAT TGT AAT GAG CCT GTT GGG GTG ACA 805
D K F E N R K H I E F S F Q P V C K A E 170
GAT AAA TTT GAG AAC AGG AAA CAC ATT GAA TTT TCA TTT CAA CCA GTT TGC AAA GCT GAA 865
M S P S E V S D * 179
ATG AGC CCC AGT GAG GTC AGC GAT TAG 892
GAAACTGCCCCATTGAACGCCCTTCTCGCTAATTTGAACTAATTGTATAAAAAACACCAAACCTGCTCACTAAAAAAA 971
AAAAAAAAGGGCGGCCGC 989

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Fig. 1



50

1 MEICRGLRSH LITLLFLFH SETICRPSGR KSSKMQAFRI WDVNQKTFYL  
 IL1ra-human  
 T77-human  
 IL1b-human  
 Consensus

51

RNNQLVAGYL QGPNVNLEEK IDVVPIEPH. ALFLGIHGGK MCLSCVKSGD  
 IL1ra-human  
 T77-human  
 IL1b-human  
 Consensus

101

ETR..LQLEA VNITDLSNR KQDKR.FAFI RSDSGPTTSF ESAACPGWFL  
 QSHPSLQLKK EKLMKLAQK ESARRPFIFY RAQVGSWNML ESAAHPEWFI  
 K..FTLQLES VDPKNYP..K KMEKRFFVFN KIEINNKFESAQFPNWI  
 IL1ra-human  
 T77-human  
 IL1b-human  
 Consensus

150

CTAMEADQPV SLTNMPDEGV MVTKFYFQED E-----  
 CTSCNCNEPV GVTDKFENRK HI.EFSFPV CKAE MSPSEV SD  
 STSQAENMPV FLGGT.KGGQ DITDFTMQFV SS-----  
 IL1ra-human  
 T77-human  
 IL1b-human  
 Consensus

192

151

CTAMEADQPV SLTNMPDEGV MVTKFYFQED E-----  
 CTSCNCNEPV GVTDKFENRK HI.EFSFPV CKAE MSPSEV SD  
 STSQAENMPV FLGGT.KGGQ DITDFTMQFV SS-----  
 IL1ra-human  
 T77-human  
 IL1b-human  
 Consensus

FIG. 2

>Contig1  
GAAGTGAAGATATAATGTATAGTAGTAATATATAATGTTAGGTGAATTAA  
AGGAAATAGAATATATTGGGGAGTAATTATGGGTGTAAAGAAATATAGTA  
GGGAAGTATTTAGATTTGAGAAAAAAGGAATTTAGTGTAGGTGAA  
NAATAAAAGNANAAGGTTAAAAATTTAAAAAATTTAAATATAAATAAAT  
AAATAAAAAATAAAATAAAATAAAATTTAAAAAATTTAAAAAATATAA  
AAAAATAAGAAATGGAAGTGGATTCTTAGAAAAAAGAAAGTAAGGTGA  
TAAGAGGAGATAGAGAGGATGTGGTGTGAGATGATTGGTTTAATTAGAAA  
ATAGGTTTTGAATAGAGTGGGAAAGTAGAGTTTGGTAAATGTGGGGGGA  
AGAGGGTAATGTTGTTTGAAGTGAAGAAAAAATGGTATATTTTATAAAA  
TAATGAGGAAAGTGTGTGAAAAAATTTATTTGGGATTGGGAAGGTGAT  
ATATAAGTTGTGGAAAAATTTGGGGGGTGGGGTTTATTTAGGATTAAAAA  
GTTATTTAAAGAAATGAAAAATGAAATTTTGTGTAATTTGGGGATAAGAA  
ATTAATGTTTGAAGAAAGGGAAAAAATGAGAAAAAATTTAGATTT  
TGGAAATTTAAAAATTTGTGGGTGTAATAGGAAGGATTTTAAAGGTA  
ATTGTGAAGGATTTGTGTGAAAAATAAGGGAGAAAAAATGGGG  
>Contig2  
GCATCTAACTGGAGCCTGCATTATTACAGATTTAGCATCACCAAAGTCTA  
AACAATTAGACTGACTAAGGCAGAACTGCCCTTATGACAGCAGACATAAG  
AAGGAAAAGGCCAAACACTGTGTTAAAAATTTATCCAAATGTGAGGAAAA  
GGCAAAGAGAGTAGGTGTGCTTTTAGTGTCTAAGCTGCCTGCCCAAGG  
GGCATCTGATGCTCTCAGGCAGGAGTCCACAAATTTTTTTGTAAAAGA  
TCAGATAGTAAATCTTTTCAGCGTGAAGAGCATGAGGTCTCTGTCAAAA  
TACTCAACCACCATTAACATGAAAGCAGCCAACAGACAACACATGACA  
AATGAGTGTGGCTGTGTTCCAGTAAATCTTGATTACAAAAACAGGCAAGA  
GGCCAGAGCTGACCCATGGGCCATAGTTTGCTGACCCCTTCTGTAAAGGA  
AAGTATTTTGTGTTGACTGTGTTTACCATTGATTGAACACAAGGCTCT  
GTAAAGTTACTTGTAACTTGCAGAGATTGATGAGTGGCAAGTAATTTT  
TATTCACCAGAAATAAAAATTTCTGTTCAGTAGAAAAAGATAAACCAA  
CTGTGATATTATGGTCCTG  
>Contig3  
GGGGTGTCTGTCTACCATGTGCTCGCAGTTCTGTAATAAATGTTCTCTCA  
AGATCCTTAAATCTCTTGGAAATTATAAAAATTTGGAAGAGAAGAAC  
AGTTTTTAAATATATATATATATATTTTTTTTGGAGATGGAGTCTT  
GCTCTGCTGCTCAGGCTGGAGTGCAGTGGCGCAAACCTTGGTTCAACCAA  
CCTCTGCCTCCCGGTTCAAGCGATTCTTCTGCCTCAGCCTCCTGAGTAG  
CTGGGACTACAGGCGCCCGCCACCACGCCAGCTAATTTTTGTATTTTTA  
GTAGAGACGAGGTTTTACTATGTTGGCTAGGCTGGTCTCAAACCTCTGAC  
CTGTGTGATCTGCCCCCTTGGCCTCCCAAAGTGTGGGATTACAGGTGTG  
AGCCACTGCACCTGGCCAGTTTTTAAATATATTTTTTAAAAACACTTGAA  
TAAGAGTCAGTGTAACCTAGAAAGTTTAAAAATGCTTCACAGAACACCCAG  
GGTTTACATTACAAGATTCTCACAACAAACCTATTGTAAAGGTGAGTAAG  
GCATGTTATTACAGAGAAAAAGTTTGGGAGCAAACCTGTAAAAAATATAT  
TTTTGTGTATTTTCTAAGAGAAAGAGTATTGTTATGTTCTCTAACCTC  
TGTGATTACTACTTTAAGTGATTTCTTGAGAGCACATGATGATCC  
>Contig4  
GCCGTTTCATAGAAAACCTGAAAGCAATAAGATGACTAGGTAAGCATGACAT  
TTAAAAGGTATTATGGGACGTGGTTACAAAACCAACTCACAACATAAAAA  
GTCTTAGGACCTCTCGCTGACTTAGGAGCCTGATCCCAACTCTGAGAATG  
ACTCAGTGTGTTACCCTGTGGCTAGTGTAGACCAATGATCCTGTCTCAGA  
GTCACCTAGCCACAGCCCATATCAAGTACTTGAAACTTTGACTCAGAAAC  
CTCAGTGTGAGAACCTTTGACCTAGGAACCACTGTAGTGGTTAACTGCA  
ATTTGCACCCCTTAGTTTCAAGGCTTTACAAACCCGGGGGCGGGGAGGGGA  
AAGGCATANANCTGATGACCTAAAGGAAACCCATTGCAGCAACGCTTTTG  
TGTTAAGTGTACAAATAAGTGTGTTTTAGAACTCTCCAGGTAATGCCTT  
TTACCTTGTAATCCAATTTGAAATGTGTAATTGACATTAGACTTCTATT  
TGAATTTGAAATGCTTAAACCAATGTGGTTAAGTTTGTAAAGGTGTGTG  
AATTTTGAAGTCTGTTACTACATTTTTTTTAAATTTCTTTTTTTTGG  
AGTTTTAGGGATTGCTTAGATGGCTAGAAAGATTTTATTCATCAGATTTT

FIG. 3 (1 of 52)

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TAAGTCTGCCTTGGCAGGCACCTTGCAGCTTTGAAAGAATCAGATATATC  
AAATTTGTAGTTTAAATATTTAAGGGAACCTCAATTAACATGCTAGAAA  
AGAGAATTAAGTATTTAGGAGGATTTAATATGGTGTGAAAGTTGTGAAAA  
TCAAAATGGAGACACTAATGTTAAGAAAACCTGATAAATGGAACCGGG  
AAAGGCATGAAGATAGAGTTCTCACACTTGTATCCCTGATCATGAAAAAG  
ATCTGC

>Contig5

GGGTTTTTCCGCGTTTTTACCCGAAATCTTCAAGGGATGGGAAAAAGAAA  
ATTGCTAAAAAATCTCGGTTTTTGGTTTTTAACAGATATTTACACNTGG  
ATCCCATTTATTATGTTGTCCCAAGGTTTTTGGTGGGTTCCCAATCAGT  
TAGCCCCCTCCACAGTGAAAGCACTTTACTTTATCACCTTCACCTAAAG  
CATAAAATCCAGCTCTTGAAAGCTGCTCCTTGTTAACTGAATATATCCAC  
ATCCCAAAAGTAATGATCCATGCTTCATAATCTGCCACGGATGGATGGAT  
GGATGGATGGATGGATGGATGGATGAATGGATGGATTGATTCTTG  
GAGGATTTGTTGAATTTGGGAAATTCACGCCAGGACAGCTGGCCCCAAC  
TGCCCGCGACAATCTGCTCGGTACAAGGGGAGGGTCTTGAGAGGGTGCG  
GCCCGAGCCCCAGTTTGGAATGCCAATTGGCTCTGCAGCCGGCCTTA  
GCCACTTGGGTCTGGCGTCCCTCATTATTAGCGCCATGCCGGCTCGGG  
TGCTGCCAAGTCCCTGAGAGCAAGCC

>Contig6

CGCGCTCAAGAAAAGCTGAAGTGTGAATGTTCTGTCTACCTTCACAGTAA  
ATGCTAAGAGAATGACCCAAGAGCAGAGGGTATCACTCTGCTACGGAGGA  
TTGATTGTAAGTGGCTCTCCTGCCTTAGCAAGAAATGCCAGAACCATGGT  
CATTCAGTTCTTGACCAAAACTGCCTTCATGAGAATCAACTTCCCCAA  
GAAAAAAAAGCAGAAACAGGCAAGCTTCCAGCATGGTAGGTAATACTG  
ACCTTCTTCCCTCCTTCTTTGGAGATTCACACAGTAATAATGCATAAA  
GCTTTGCCAATGGACTAAGCACTGCCAGGGGTTTTTGTCTGCCTGGAC  
TGAAATGCTCTTTTTCGTTATCATAGAATCCAGTGCACTCTGAGTAGA  
CTCTAAGCAAAAGGGACATTTTTCAAAAAGGCTTTAAATTGCTAGTACAA  
AGAAGGCAACAAACTTGCGTAACTGTGGACAGATTAACCTCACTTGGTGT  
TTTGGCTCTTCAGTTTTCCCTTGGCTGCCAAGTACTCTGAAGCTTTCTC  
TGCGGCTCTTCTGCAAGCAGGCAAGCAAAAAACGACTGAACCTTTATTT  
CGAGAT

>Contig7

GAAGAGCCGCTAACTTGCTGTAGTGATAAGGAATGAACCTAAGGCTAGGGA  
CATATTAACATCCGCTGGTGGTGAATCTTTAGCCTAGATCTTACCCCACT  
CCTGCTCCTTCCATATGGTTCGGTCTCAGGCTCACTACCGATCAATGGCG  
TACTAAAAGCACTAATAGACTCCAACACGTCTGTCTGTGTTTACG  
ACAAGCCGTGGAGTTAATCCCTCTGACAGTAGCTCAGATAAGGATGGCT  
ATCATGGGCCCCGGAACCTGGGGCATGACGCTCGTCACCAACGCATGAGCTC  
CCCAAGTATGCTATACCTGTCCCTATGAAGGGCTTCCAACCTCTATGTGCA  
GTCCCCATGTGGAGAGTCAGGTATTGATTGATCAAGCCAGGGGTGTGGTG  
AATGGGGAGCTTCTACAGGGGTAATGATAATTGAAATGCACGGTGATGG  
GGATTTTCATATTGGTCTCCTAAGGAGATAACAGATTGGATGCGGGGTGCG  
ATATTCCACTGCCAGGGTGTGTACCGAGGGTATCTGCAGGTGGATCTCC  
TCCCCACGTTTGATTAATACTCCTGTCTTGGGAAGCATAGACGGGCGGGG  
GAAATGATGAAGGGTGACCACTCCCC

>Contig8

GGGAACGCAGTGCTCTGTACGATGGCCTTGATTGCGAATTCCTGCAGGGG  
GGG

>Contig9

GGCAAGAGATTTAATATTCATTCCATCTTCATTTGGAAGATGAAAAATTG  
GGGACCAGAGAGGGGAGGGGACTGGGCCAAGTTTTCAAAGAAAAGTCAGT  
AGGAATTGTGAATTCCTGGGGGCCGGGGCCATTAGTGCTGTTTTGGATC  
AGTAAATGGAGATGTGAGTTTCAACAGTAACAGGGACATTTTAAATTA  
AATGATTTAACCTTTAGAAAAATGTCCTATTTTGTAAATGATGGATTCA  
CAGGAAGGTACAAAGAAATGTCCAGAGAGTTCTGAGCCCCCTTCAGCCA  
GCTTCTTCCAATGTTAACATCTTGCAATTATTATAGTACAACATCAAACT  
GGGAAATCGATATTGTTACTGTCCAGATAGCTTACTCAGATTTTGCCAGT  
TATACTTCCACTCATTTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGT

FIG. 3 (2 of 52)

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TGTGTGTAGCTCTATGCAATTTTATG1...GTAGCTTCATGTAACCAACCA  
AATCACAATACTTAACTATGCCCTCATCACAAGACTCTCTCTTGCTATGC  
TTTACAGCTGTATCCTCTTCATCTCCAAACCCTAAGCCCACTCACCAGCC  
TCCACCATCTCTAATCCCTGGCAACCCTATTCTGTGCTCCATCTCTGT  
ATTAATTGTGTTAATTAATGTTATACAAATGGAATCATGAAGTATGTGTC  
CTTTGAGATTGGGCTGTTAATTTTTCACTCAGCACAATTTCCGTGAGTCT  
AATCCAACCTGTGTGTAGCAGTAATTCTTCTTATTATTGCTGAATAAT  
ATGCCATGGTATGGATGTATCACAGTGTGTCTAATCCTTTGCCCATTTGAA  
AGGAATTTGGATAAATTTCCAGGTTTGGCTATTATGAATAAAGTGAACAT  
AAGACATGTGTGTACAAATTTGGTGTGATCAAAAGTCTCATTCTCTGG  
GATAAATGCCCGGTAATGAAATGGCTGGGTTGTGTGGG

>Contig10

GCAAGAACACAGGCGCGTATTATAACCTTACTACCAAGACCTGAACCCAT  
ATAAAGGTTTATGCGTAACAATCATCATCCCTGTTCCAGAAGATTACAG  
TACGACCACGCTGCTCACCAGCTCAGGTGGGCCAGTACCAGAAATTCT  
CCCAACAAACAGTCGTGTCTGAAAACAATCGCGGTGACCTCCACGGTTA  
GAAAAGCCTGTTTTCAAGTCTGGAATTGCCACATATTAGCTGGGTAAT  
TTGGGCATCACATTTACTCTCTCCGAATTTGAGATTGCAAAAACCTCATTG  
GATTGTTTTGTGGATTGAAAGAAATAATGTAAATTTAGGCCGAGTGCTTT  
GACTTACGCTGTAAATCCTATCACTTTGGGAGGCCAAAGCAGGAGGGTCA  
CTTGAGCTCAGGAATTTGAGACCACCTCTGGCAACATAGTGAGATCCTGT  
CTCTACAAAAAATTTTTTAAATTTATCCAGCATGGTGGTACACGCTGT  
ATTCCAGCTACTCAGGAGCTGAGGTGTGAGGATTGCTAGAACCCTGGGA  
SATCAAGTCAACAGTGAGCCGTGTTGTGCCACTGCCCTCCAACCTCAGT  
GACAGAGGAAGACCCTGTCTCAAAAAAAAAAAAAAAAAAGTAGTAAGTTTAA  
AGAACTTAGTGAGGCTGGCATATAAATGATATTGTTGATGTTGATGTT  
AGCTTGAAGGCACATTTATAGGAGTAGGGATTTTATAACATTATGAGCCT  
GAGAGCACATATAATGTTCCC

>Contig11

GGTCTAACATGCTCCAACCTGAAGAAACCCACACTTGTCCGGCAAGGAAA  
CTACTACAGATTTCTGACCTACTGTGCAATTCGGGGCATGCGACGGGAC  
TGTGTTTCTGGGTACGCTGTCTCAGGTTCTGTGGGATGTAAGAATTCAA  
CTTCAGTAGTTCTCTCATAGACGCCGACGAGAGGGGCGTCTTTTTCTCT  
GATGAATCTGCCAGATCTTCCACTTCATAGAGTCTAAATCCTCCGATTCTG  
ATCTACTGGAGACCCACGTTACAAAACGCTCTAACGTCGGTGACAGCT  
CCCCACATAGGGAAAGATCACCTGAGTCTCACTACCTCACATTAGTGCTA  
TCTCCAGCCCCATGCTATCTACGAGATGGTCACGCGAGGTTTAAAGGGGTC  
TCCGATTCCGGTGGTCCGATTGAGCTAATCGTGGCCCTACGTGAACGATC  
ACTCTGCTCGTAACATCGATACAGGGTCGCGCTGACAAATGGTACTACG  
TAGGTTCTCAGGTCAATGCCGCGTCACGAATGAGCCTAACTACCCATAA  
GTGCACGTACTGTGTACCTTTCTGTTCCGGCAAACCTGCTACTGTATG  
CTGTGCTTGTTT

>Contig12

AGGCTCCATGTGCTCTAGCCTGATTATCTTTTTCAAGTGTTTTATTGCTA  
ATCTATAAGGCCCTTTTCGTAAATGTTCACTCATTCTTAATTAGATAT  
TTTTTTAATGTTGAGTTTTGAGAGTTCTTTAGATATTTTAGATACAAGT  
CCATTGTCAAATATGTGATTTACAAATATTTCTCTCAATCTGTAATTTA  
GTTTTATCCTCTTAACAGGGTCTTTTGGAGAGCAAATAATTTGATTTTC  
ATAAGGTTCAAATTATTAATTTTTCTGTATAGTTCACTTCTAGTGT  
TAAGTCTAAAACTGTGCCTTGTCTAGGTACCAAGGTTTCTCCAGTT  
TTTTTTCTAGAAGTTTAGAGTTTCATGTTTTACATTGGAGTCCATGATCC  
ATTGTTAATTAATTTTTGTATATAGGTAGATGTTTAGGTTTAGGGTTTTT  
TTAAAAAAATTAATATGTTTAAATTGCTCCAGTTCCCTTTTATTGAAA  
AGGGTATCCTTCCCTCATTGAATTGCCTTTGTGAGAAATTAATTGGACAT  
ATTGTGTGAGTCTATTTCTGGGCTCTTTATCATGTTACTTTAAAAAAT  
GCATCAGTTCCCTCCCAATACCTCATTGTCTTGATTATTGCAGTTATAT  
AGTAAGCCTTAGCATTAGGAAAAGTGTTTTCTGCTTTATTCTTTNTCA  
AAAAATTTTTGGATATTCTAGGGCCTTTACATATAAATTTAAAAATACT  
TTGTCTATGTCTAACCGAAAGCCTTATGAAGATTTTGATAAGAATTGCAT  
TATGCCATATACATTAATTTAAAAAGAACTGATGTCTTTATTAGTTGATT

FIG. 3 (3 of 52)

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CTGCTAATCTATGAACA1AGCATCTCT...CAAAGCATTTAGTCTTTCTT.  
AATTTCTGTCATTAATTTTTTAAAAATTTTCATCCTAAAGATTCTGTATAT  
GTTTTGTTGAATTTATGCTTAAGCATTTCACTTTCTTGGTAACAATTATA  
AATGATTTTGTGTTTTTATTCCACTAGTTCATTTTCAGTGTGTAGAAAA  
GCAATGAATTTTGTGTGTTGATCTTTGTTCTACATCTTGCAACATTAT  
TGAACCTCATTATTAGTTCTAGGAGGTTTTTTCATTTTTCTGTAGATAC  
CTTGAGATTTTCTATATAGACAGTCATGTTGTCTGCAACAGGCACAGTT  
TTATTTCTTCTTTTCAATCTATATGCCTTTTTTTTTTTTTTGCCTTAT  
TGCAGTGGCTAGAACCTCTAGCACTATGTCAAATAGCATTGGTGAAAGCA  
GACATCCTTGTTCTTGTCTTAGAGGAACATTTGGTCTTTAATCTTGAT  
TGCG

>Contig13

CGGCCTCCTTTCTCTTCCAAAATTTCTTGTCTAGTTATTTGTCCAGG  
GAAATTTGAAAGCTCACTTACTGTGCAAGTCAGCAGGAAACAACCTGGGTC  
TGTGCACAGCACCTAGCAAAGTTCTGCTCTAGGAATTACACTTTGGCCCT  
GAGGTAGATTTCTACAAGAACCTTACCTTCTAAGCAGCACTGGGGTTCAT  
CTTTTTCCAGTCTCTCAGAGCCCATTTTCACTCCTGAGTTCTCCCCACA  
AAGGACATTTTCAACGTTGAGTTTATTACTCAACAGAAAAATGGAATGAAG  
TCCAAGACCTAAGGAGATAGAAAGGGGACCAGTTATGGCATCTTCTCACC  
CCAGGACACCTTGCTGCATGTCTTAGTGCTGAACAGACCACTGGCCTTG  
CTCTGTAGTTTGAAATGCTCGCTGCAACCAGAAAGGCACCAAGGGGCCAG  
ACCATGCTCTCCTGTCTATCACGCCTTCAAAGCAGAAATTTCCCAAACCTT  
GAGTCACAGTGCTAACACACGGGGTGCCTAACATTTTGTGATTTTGG  
CATTTTACAAAAATAAAATAAAAAAGTTAAAAATGCATTGCTCTATTCTT  
GGGGCTGGCACACTATTGCCTTTGGCCAAATCCGGTCCCTGACTGTTTTT  
TTAAATAAAGTTTATTGAAACACAACCATGCTCTTGTGTACATATTGTC  
TCTTGGCTGCTTCGAAGCTACAATA

>Contig14

GTGTTGCTTTTTTAACACTTACCTAAAATTACTCTGTAATCCATGGATCC  
TTAATTTATTTAAAAAATAATGTTAATGAGTAGCTTTATTTTCTCCCA  
TCTAATTTAAGGCCACAGAACACCTTCACTTACCTCAATCCTCTCCCAA  
CTTACATGCTTTTAAATGTCATATATGTTAATACCGTATACTTTTAAACT  
TTCTAAAATAGCATTATTTTATAGCATGAGTGTTCAATTACATTTTGTCA  
TATATTTAGAATTTTCTTGTCTCTTCGTTTCTTCTTCTATTATGACTCC  
CCTCTGGGATCATTTTCTTCTACTTGAAGTACATAGTTTGAAGTGCAC  
TATTCAATACAGTAGCCACTAGCCATGTGTAGCTATTGAAGTTTAAACTA  
AGTAAATTTAGTAATATTAAAAACTCAGTTCTTCTCATCTCACTAGCCAC  
ATTTCAAGTGCTCAGCAGCCACGTGCGACTAATGACTACTGTACATCAAA  
CATATAGAACATTTCCATCATGGCAAAGAGCTCTATTGATAGTGTTTCATC  
CAGAGTTTCTGTTCCAGGACCAAACCTGAGGGTTGGGCTGCTATTTCTCAT  
GGCCCAATAACAAGATGCAGATGAGCTGGGGAGGAAGAGAGTTTTTATTT  
CTGCNACCATTTACCGGGAGAGGCTGGAAATCATCACCAGGCCAACTC  
AAAATTATTACGTTTTCCAGAGCTTATATACCTTCTAAGCTATATGTCTA  
CGTGAAGTGTGCATTACCTGAAGACGTTAGTGATTAACTTCTTTTAAAT  
CTGTAACCTAAGGCTGAGTCCGGAAGATCTTCCCTGGAGCCTCAGTAAA  
TTTACTTAACTTAAATGGGTCCAGGTGCTGGGGTAATTACCCTTATCTTG  
TCCCCTGCTAAATCATGGAGGTTTGGGGATTCTTTAGAGCACCAATAAA  
CTTGTTTGTGGAGGCCTGGGGGTTTTCTTCTGACCCACAATAAACTTGTT  
TAATCCTAAATGGGTCTGTAAAGAAATCCTTCTTTATTTTGTATATTT  
TAAGGCCAGAAAAGGCCTGGGCAAACTCTTGATGGGCTTTTGTACAT  
TCCAGCCTTTGTATAAGAACAAGTGGTTTTTAAATTTAACTTAACCATTT  
AGTCAGTACTGAAACAGTTGTTATAGAGATCTGCATTAGTGAGACCTGGC  
CTGCCACATTTCTTTTCTGAAGATCTTATGGTAGTGATCACCTTTGTGA  
AAGGAAAATAAATCTTGGGACCTCAAAATCACTAAGCCAAAGAAAAAAGT  
CAAGCTGGGAAGAATCTGACACTTAAATCCAACACTGCTAACTCATTCAT  
CTCACTCATTCACTTATTTTCTTTTCTTTTCTTTTCTTTTCTTTTCTTT  
TTTTTTGAAACGAAGTCTTGTCTGTGTCACCCAAGCTGGAGTGAGTGAT  
CTCAGGTCACTGCAACCTCCACCTCCCGGGTTCAAGCGATTCTCTACCT  
CAGACTCCTGAGTAGCTGGAATTACAGGCACCTGCCACCACGCTGGCTA  
ATTTTATATTTTATAGTAGAGACGGGTTTACCATGTTTCATCAGGCTGG

FIG. 3 (4 of 52)

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TCTCGAACTCCTGACCTCGTGATCCGC...CCCCCTCGGCCTTGTTTGCT.  
GAGGTACTGTCTAAATGCTGGAAGTGAAGTGGCAAGCAAGACATCCCTA  
CCCTTGAGGAACTGTAATCTAGTCGGAAATACAGATGTCAACCAAGTCT  
CACACAAGAAATTTGTACAAAACCCCTAGGA

>Contig15

GGAAAAACCTATCACCGCCTCCTATGGAACCTAAAAACAAAAAGAAAAGTA  
ACAAAGGAAATGAATATTTTCATTCTGGAAGAACATTGAAAAAGAACAGGA  
AGAAAGAGAAAGCACAACCTCGAAGTGTCCACTAGAATTGACAACACTCTGA  
CAGAATGTCTGAACCTCATCGAAGGGGTAAAGTGAAAAAATAAGCTCCTC  
CAGCTTTGGCCCAAAGTCTTATAATTTTTAAACATATTCCTAAATATAAT  
ATAGGAGAGATAGCCTTCATCTAAGTAGAAATTTAGCTACTCTTGTAAT  
ACAGAGTAATAATAATAATGACATGCCATAAACAGTGTCTTTTGTGTAT  
CTGTGCTTTTATAAGCACTTAGCTAAGATTATCTCACATAATTATCATAA  
CCACTGTTACTATGACCCTTTACAAACAAAACCTGAGGCACAAAGAAGTT  
GGAAACTAATCCAAACAACTGGCTCCAAAAGGAACTTTGCTTTCTTTG  
GGTATCAAGTTCTGAAGAGTACACATTTAACATTGAACTGAGGTCAGAA  
GGCAAGTTTCTATGTAAAGTTGGAGTATTCTGAATACTCTGGGTAGCTAC  
AAATAGTATTTAAATTTTATCTTGGATTCTGCAGATAAGGATAAAATAGA  
TGGTAGGCAAAGAGTATGATCCTTAGGAGAAATTTTCTGAAGGAAAAA  
TATATTAATAAAAAATGATGGAATAAACTCTAAGATCCTTGCCTAGAGC  
AAAACCTCATTCAAGTCCTTTGGCTGGTAATGTTGAACATCAACAAAAA  
GGAAAAGTTCAAGTTTAAAGTCTACTCCAGGCAACATTTTCACAACATCCAG  
TTAAATATTAACATTTTCTCTTTGTGGAATTGAACTAGAGTTCTTTTCT  
TATCCTCTTTTGGTTGTTGTATTATTTAAAAATGAGTACCTTTTAT  
ATTGAAATCATTTCAAGTAATGCAGATAAATGATCAGCCCTCTCCCTGTA  
CAAACATACATACTTAGGCATCCCAAACCTTCTCTGGAGGTGACCACCA  
TTGCCAGTCATTCTGTTTTCATGCATGTCCATACAGTATAGGTATG  
TCGAGAAATGAAGTATTATATTTTGTGAGTTGCAATTCTTTTATTCACA  
TTTTTGTGTACTTTGGTTGTCTTTTCTGTGTTTTCTAGTACCAATGTT  
ATGCTGACTTAGGCAGATGAGTTGAGTATTTTCTTTTGGCCTATAAAC  
TGAAAATAGTTGTATGACATGAGAATTATTTTATTTTGAAGGTTTG  
ATAAAAACCTTGCCCATAAAAATCGTCTGGACCGGTTTCTTGAGGATGCCT  
GTGTTAGAGCC

>Contig16

CGCTTTAACCTGGGCTACCAATGGTTCGTCAAGTTCTAGATTCTCTATTA  
ATACCTTTTCTTGTGTCTTTCTCTGGTCTGTTTTAGCCCCGAGTCTCT  
TAGATCTGTCTCTAATATTCCTATTGACTTTACTTCATTTTCTAAGTCT  
TTATCCTTTTGCTTACTTTCCGAGAGACCTGCTTAACCTTATCTCCAA  
CTCTTTTATTGAATTCATTTCTTTTACTATATATTTTACTTTGAATA  
CACCTCTCTCTTCTCACATTTTCCCCATAGTATTTTGTCTTCAATTGA  
CAGTCTACTATCTTATTACTCTGGAGATATTAATAATAGTTTTTAAAT  
TTTATTTATTTTTATTTTCAAACAGTGTCTTACTCTGTCACTCACGCTG  
GAGTGCAGTGGTGTGATCATGGATCACTGCAGCCTTGATCTCTGAGCTCA  
AGCTATCCTCCTGCTTCAGCCTCCAAGTAGCTGGAACCAAGGCATGTG  
TCACCATACCCAGCTAATTTTTTGTTTTTGAGGTGGAGTCTCACTCTGT  
AGCCCGGTCTGGAGTGCAGTGGTGAATCTGGGCTCACAGCAACCTCTGC  
CTCCTGGGTCTGGTTCAAGCAATTCTCCTGCCTCAGCCTCCTGAGTAGC  
TGGGATTACAGAAACACACTACCATGCCCAGCTAATTTTTGTATTTTGT  
AGAGACAGGGTTTACCATGTTGGCCAGGCTGGTCTTGAACCTCTGACCT  
TGTGATCTGCCACCTTGGCCTCCCAAAGTCTGGGATTACAGGCGTGAG  
CCACTGCACCCGGCCACTAATTTTTAAATGTTAATAAAGACGAGGTCTT  
GCTATGTTGCCAGTATGGTCTTGAACCTCCTGGGCTTAAGTAATCCTCCT  
GCCTCAGCCTCCCAAAGTGTGGGATTACAGGTGTGAGCCACTGAATCTG  
ACATTTTTTAAAGTTTTTCTCTCTTTACCAAGTCTTTTTCCCTTTCT  
GCTTTTTTGGGTTGTTTTATTTTGTATCTCTATCTTGCTAGAACTTTCTG  
CAGACGTTTAGTAATACTAGATTTTTGAGAGTGGGCAACTGGAAAGCTGA  
TTGGAAACTCTGAATACATGGGTGAGGCTTGTGGCTGTGAGTGTCAATG  
CTTGATGTCTGGCAAGGCCAATGGGTTTGGGACCCCTACTATTAGTATA  
GGCCTGATTCCCTGGGAAAGGCTCTTTTGTATCTCCTGCCTGGAGGATAAA  
GGCCTGGCTACCAGCCTTCTGTGTGTAATGTGAGGGAGAAGGGCTGGAGT

FIG. 3 (5 of 52)

ATTCAACATCATGCTGAA.CCTTTCAA.LATCATCTTGTTTTTAGTAATC  
TCCTACCTTAACTCTCTGTCTTCTGCTAGTATGGGAAAGATGACCTGAAA  
ATCTAACCATTTATTTTTCCCCCATTAAATATCATTATGATTATTGAGA  
AGTTAAATAATTGTCTGCTGCTCCAAAAAGACTGAATCAACTAGCAA  
CAATAAGAAATTTCTCACAGCTCTGCCAGCATTTTAAAAGAATAGCTTT  
ATTGAGCCCAGGAGGTCAAGGCTGCAGTGAGCTGTGATTACACCACTCTA  
CCCCAGCCTGGGTGACAGAGCAAAACCCTGTCTCAAAAAAGAAATTTAAG  
GAACAGCTTTTATTGTTGTAATAAGACATACAATAAACAGAGCACATATT  
TAAATTGTGCACTTATACTTTGATATAACCCTGTGAAAACATCACCACA  
ATCAAGATAGTGAATATATTTATCACCTCCTGATACAGTTTAGCTCTGTG  
TCCCCACCTAAGTCTCATGTTGAATTGTAATCCCCAATGCTGGGGGAGGG  
GCTTTGTGGGAGGTGATTGAATTGTGGGGGTGCACTTCCCCCTGTCTGTT  
CTTGAGATAGTGAATGAGCTCTCATGAGCTCCCCCTCACTCACTCTCTTT  
CCTGCTGCCATGTGAGGATGTGCTTGCCTCTCTTTGCCCTTCTGCCATG  
ATGTGTTTTCTGAGTCTCCCTAACCATGCCTCCTGTACAGCTTGCAGAA  
CTGTGAGTCAGTTAAATCTCTTTCTTCATAAATTACCCAGCTCAGGTG  
GCTCTTTATAGCAGTGTGAAAAGGAACTAATATACCTCCTAAGTTACCTC  
AAGCTTGTTTTTAATTCCTTCTCCTCCCTTCCTTCATTGCCAAGCAAACA  
ACCACCTGTTTTCTGTCACTATAGATTAGTTTACATTTTGTGGGTTTTTT  
TTTTTTTTGAGACAAGGTCTGACTCTGTTGCACAGGAGCAGAGCAGCGTA  
TC

>Contig17

CGCGTTATAGGAGATGCGAACCTTAAGAAATGATGATAAGGAGACTTTATT  
AAATATAATTTGAATTATTTTGCCATTACAGAAATCTAATTATTTAAA  
ATTCTATTACATAATTTTAACTACTGTACTTCCCAAGCTTAGCTTAGAAT  
CCTTCTGTGCTGAGGATTAATTTTAAATTTGTCTTTTATAGGCCTTATCTA  
AAATCCAAGAATAATTGCCAGAATCAACCACCTTCTAAATCTGTAAGTAG  
AAATTAGTCTTTTTTAAAAATATGCATTACATAAGTATGATTAGTAATAAAA  
ATAATAAAGATGTTAGCAACCTAAAGAACATGATTTGAAAGGTATTTCT  
TACAGATATAAAAAACAGTTTGGTTTAAATAAGAGACAATCATTTTTTGA  
AGTATGACATTTTTTGAAGAGTAGTTTAGTTTTATTAACCAAGAAAAGCC  
TCAAGTGAACCTTTAGTCTCTTGATAGCTAACATTTATTGAATGCTTACT  
GTGTGCCTGATACTTTTCTGACTTGCATTACCTCACTGAGTCTCACAAT  
CTTATGAGGCTACTATTAGTAGCCCCACTTTACAGATGAGCAAACTAAGT  
CACAGAAAGGTTAAATAGGTCGTATAGCTATTAAGTGACAAAGCTGAGAG  
CCTGTGATCTTAACCACCTTTGGTATGCTGCCATGAAGTTAAATAGCTCAG  
TAGTCATTAAAGAGAAACATTTGCATTGAACCTTCCAAGCCACTTAACAA  
GTATATGCTTCCTAATCAATTTAATTTAGCTACATTAGATAGAATGGTAA  
AGGATCCTTAACCTAAAGTTTAAATGGAAGAAATTAGCCCTCTGAAAGAG  
GCACAGATTATTCATCTGCAATAAAAAATCTCACCTTTAGTTTTTAAAC  
ATAGTTTTTATCTGTGTTCTGAAATGTAACCTAAACAGTGCTTCTGAAG  
TGAAAAAATTCCTCACTGGTGAGAAATTTAATAAGTTTAAATGATTCACCAA  
ATCACTTCAGTCATATTTCACTCATATGCATATGCATATATAGACATATA  
AGTTTTTATCTGTGTTCTGAAATGTAACCTAAATAGTGCTTCTGAAAGTG  
AAAAATTCCTCACTGGTGAGAAATTTAATAAGTTTAAATGATTCACCAAAT  
CACTTCAGTCATATTTCACTCATATGCATATGCATATGTAGACATATATA  
TGTTGTATGTATACATGACATCATTAGACACTGTGAAGGATAGCAAAATG  
TATATAAGGCAAAATTTATGAACAATGGTTTAAACGTTTGGGAAGCACTGG  
GTTACACTTTTACTTTATGCAGATTGAACCAGTATAGTATGCAAGTCTTA  
AGGAAAAATCTACTGGAAAGGGCCCTCATTCACTTCCCAGAGGCTTCT  
CTGGAAGTTGACAATACTGACTTCAGTACATCAGCTCGTAAATGAGGATG  
ATACCTACCTTATCTGCTTTACACAGTTGTAAAAGTAAAAGTGAACCTCA  
GGAAGGGAATTACAGAATTTAGGAGAACTAAAAGCACGATGTAAATAAT  
AGTCATCATTACAGTTATATAATGCTTGACAATTTATATAACACTTTTGA  
TACATGACAACAATAACTAACCCAGACATGTTTATATACATTACCTCA  
CTCAGAACAACCATGTGAGGAAGTTGGCCATATGCTTTAATGTCCAAACC  
AGGACACTTTTGAAGTAAAAGCAGTACTCTTTGACCAACAGGCATAAA  
TCAAACTATCTTGTGAAAACCGGGATATATGGCATCCTTCTAGATAAT  
AGATACTTTTACTATTATTAATTTTGTCTGTGAATCTAAACCTGCTCTAAA  
AAAGTTAATTTTAAAAAGTAATGAAGTACTGATACATGCTACAACATGGG

FIG. 3 (6 of 52)

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TAAATCTTGAAAACGTTATGCTAAGTG...AGAAGCCAGACAGAAAAGG...  
ACATATTACATGATTCCATTTATATGACACATCTAAAATAGGCACATCTA  
TAGACATACAGAGACAGAAAGTAGACTAGCGGTTGCCAAGAACTGCAGGG  
AGCAGAAGATGGGGAGTGAAGTCCCAATANGAAAACGCATTACGT  
>Contig18  
TGAATCGCAATGATATGTGCCACTTTGCACTCTCTGTGACATATATAATT  
ATTTTTAATGCATTTCATTTTTCTCAGAGTGCATTTCGTTTGAAAACATA  
GACGGGAAATACTGGTAGTCTTCCTTGTCAGTTAGAAAACCCAAACAAT  
GAAAAATGAAAAAGTTGCACAAATAGTCTCTAAAAACAATGAACTATTG  
CCTGAGGAATTGAAGTTTAAAAAGAAGCACATAAGCAACAACAAGGATAA  
TCCTAGAAAACAGTTCTGCTGACTGGGTGATTTCACTTCTCTTTGCTTC  
CTCATCTGGATTGGCATATTCCTAATATCCCTCCAGAACTATTTCCCT  
GTTGTACTAACTGTGTATATCATCTGTGTTTGTACATAGACATTAATC  
TGCCTTGTGATCATGGTTTTAGAAATCATCAAGCCTAGGTGAGCACCTT  
TTAGCTTCTGAGCAATGTGAAATACAACCTTATGAGGATCATCAAATAC  
GAATTCATCCTGAATGACGCCCTCAATCAAAGTATAATTGAGCCAATGA  
TCAGTACCTCACGGCTGCTGCATTACATAATCTGGATGAAGCAGGTACAT  
TAAAATGGCACCAGACATTTCTGTATCCTCCCTCCTTTCACTTACTTA  
TTTATTTATTTCAATCTTTCTGCTTGCAAAAAACATACCTCTTCAGAGTT  
CTGGGTTCACAATTCTTCAGAAATAGCTTGAAACACAGCACCCCATAA  
AAATCCCAAGCCAGGGCAGAGGTTCAACTAAATCTGGAAGTTCCACAAG  
AGAGAAGTTTCTATCTTTGAGAGTAAAGGGTTGTGCACAAAGCTAGCTG  
ATGTACTACCTCTTTGGTTCTTTGAGACATTCTTACCCTCAATTTTAAAA  
CTGAGGAAACTGTCAGACATATTAAATGATTTACTCAGATTTACCCAGAA  
GCCAATGAAGAACAATCACTCTCCTTTAAAAAGTCTGTTGATCAAACCTCA  
CAAGTAACACCAACCAGGAAGATCTTTATTATCTCTGATAACATATTTG  
TGAGGCAAAACCTCCAATAAGCTACAAATATGGCTTAAAGGATGAAGTTT  
AGTGTCCAAAAACTTTTATCACACACATCCAATTTTCATGGCGGACATGT  
TTTAGTTTCAACAGTATACATATTTTCAAAGGTCAGAGAGGCAATTTTG  
CAATAAACAAGCAAGACTTTTTCTGATTGGATGCCTTCAGCTAACATGC  
TTTCAACTCTACATTTACAAATTATTTTGTGTTCTATTTTTCTACTTAAT  
ATTATTTCTGCAATTTTCCCAATATTGACATCGTGTATGTATTTGCCATT  
TTTAATATCACTAGACAATTCAATCAGGTTGCTACGTTGGTCCCTTGGGT  
TTACTCTAAATAGCTTGATTGCAAATATCTTTGTATATATTATGTTTTT  
TCTCCTATCTTGTAATTTCTTTGAGCACATCCCAAAGAGGAATGCCTAGA  
TCAATGGGCACAAATAATTTGACAGCTCTTATTAAACATTATTCTGTAAAG  
TAAAAACTGAACTACTTTTCACTATCACTAGCAACATATGAGTGTATCAG  
CTTCCTAAACCCCTCCATGTTAGGTCAATTATGAACTTATGATCTAACAA  
TTACAGGGTCTTATCCCACTAATGAAATTATAAGAGATTCAACACTTATT  
CAGCCCCGAAGGATTCAATCAACGTAGAAAAATCTAAGAACATTAACCAA  
GTATTTACCTGCCTAGTGAGTGTGGAAGACATTGTGAAGGACACAAAGAT  
GTATAGAATTCCATTCTGACTTCCAGGTATTTACACCATAGGTGGGGAC  
CTAACTAC  
CATGCACACACAATCTACATCAACACTTGATTTTATACAAATACAATGAA  
TTTACTTTCTTTTGGTTCTTCTCTTCAACAGTGAAATTTGACATGGGTG  
CTTATAAGTCATCAAAGGATGATGCTAAAAATACCGTGATTCTAAGAATC  
TCAAAAACTCAATTGTTTGTGACTGCGCAAGAAGAAAACCCCATGCTG  
CTGAAAGTCAGTTGTCTTTGTCTCCAACCTTACTTCTTTACCTCTCAT  
ATGTTTGTGAATAAGCCCAATAAGCAGACNCCTCCTACAAAGTGAACCTG  
GTCTCTTCTCTCTAACAGGG  
>Contig19  
GTCTTGTAACACAGGTAAGACGAGTTCAAGTTTTATTTCTTGNTTTTAGA  
ACGGTAGTGAGCGGTTTTCAGCNTGAGACCACACCTAAGGTAAGTAGCTG  
AATTGGGGTTTTGTCTTGGCTAAAGTTTAAACACAGCTGGTCTTAATTT  
CTCCTTACCATTAGAGCACTCAGTAATCATATAAGTTGTGTGATCATTCA  
TTTTGCTTAACTGTTTGTCTGTTTTATTGCTGTTTCAGTCTTTTCC  
CATTGGGTTTGACCTACTCTATCTGACTTGATCAAATCCAAAGGAAATTT  
CCAAATTATGGGGAATGAGGCCTCTGAAGTGGCTAAATCCCACCTCCC  
ACACACACAAACGTGGTATGGTGGGGGAAAAACGGCCAGCAAAAGAAAA  
AAAAAAGGAAAAGATGTTTTCAATTTGACCACCAAACGGGCTTTATTTC

FIG. 3 (7 of 52)

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ATAACAAGGCCACCTTT...GCTAGCCA...CCATACTGAAAGAGCAATG...  
TGTTGCCCCATGCTGTGGGTTCCATAGCTAACGTTCTGCCTTTTTCTTA  
CCACGACAGCCTGGGTTTGGTTTCTAAATCAAGCCTTTCTGGTTTGATA  
CTTGGAATGCTGAAATAGCAGCAATTTGTCTAGCTGAAATATCGTAAT  
AAGATTTTAAAAGATTTATTTTAAAGGACCTCAATAGTTAAAAGTCAGCT  
TAATTTAAAAGCTAACATCCAAGATGTGTGCATGTGTATGCGTCTTT  
GTATTTAAATAGCCCTCATGTTTTTTTTTCTTCTAGGAACTTGCCTT  
TTTTTGAGCAAAAGTTTTTTCTTCTGTGACTGGATTCTGTTTTCTT  
CATTTACTTCTGCTGTCTCTCTTTCTCTTGACCGTCTGCTGCATGAGA  
GCCCTAAAATAGTTTATAATAGCCTGGGGTTCCCTAAAAGAAAATGGAGAA  
GGTGCCAGGCTCCCTTTTAGGGAGAACTTCTATTTTCTTATGGAATC  
CCTAGAGTGTAAACAGACAAGTTCATTCAGCTCTTAAACTGCTTGCCTT  
TGTGTTGTGTACCTGATTTTGTGACTATTATTTTGTAGCTATT  
GCAACAGAAGCTACTCTTGGGTTTTCAAGGAAGATTGTAGTTTAGACATG  
TAGAAATGTCTTTAAAAAAAACAACTTTTTTTTAAAGTGCAGTGTAA  
AAGCATCATATGGTCTAGCCTCCTAATAATTTTCCCTTTTGGAGACCAG  
GATTGAGGGTGGGCTCTGCCCAGAGCTCAGAGATCCAGTTAAAAGAGAGG  
TAGTCTCGGCGGGCGTAGAGGCCAGCCTGTAATCCAGCACTTTGGGA  
GGCCGAGGCGGGCGGATCACGAGGTCAGGAGATCGAGACCATCCTGGCCA  
ACATGGTGAACCCCGTCTCTACTAAAAATACAAAATTAGCTGGGTGTG  
GTGGCAGGTGCCTGTAGTCCAGCCACTCGGGAGACTGAGGAAAGAGGAG  
AATCGTTTGAACCCGGGAGGCGGAGCTTGCAGTGAGACGAGATGGCGCCA  
CTGCACTCCAGCCTGGCGACAGTGAGACTCCGTCTCAAAAAAAAAAAGAT  
AGGTAGACTCGATGTTGTCTACCCGAGCAAGTTAGAGCAACGCCACACT  
TTGAGACGAATTTAAGAGTCTTTATCAGCCGCGGACCAAGAGACGGCTA  
ACGCTCGAAATTTCTCTCGGCCCTTGGAAAGGGGCTGATTTTCTTTATG  
CTTTGGTTTAGGAAGGGGAGGGAGCTCAGTTGCAACAATTCTACAGGAG  
TAAAAACATGCAAAGAAATTAAGAGACAAGTGGTTACAGGGAACAAAC  
AGTTCCAGGTGCAGGGGCTCTAAATCTATCATAAGATGTTAGGTATGGGG  
GCTCTGCCGGACACAACTCAAGGCTTTATGCTGTTATCTCTTGAGCGAA  
ATCCTGGGAACCTCGTACATTGCTTGCTTCACTACCTTATCAGTTAATCG  
GACTCTTTGATATGTTGGGAGTCAGCGTACACAAGTTAACTCCTTGAGGA  
AGGGGGTGGGTGAAGGAGTCTTGATGTCTGGTAAATGAAGGAGCGAAATC  
GAGTTCTCTGGCTTTCTCAGCTAAGGGAGAGCTTATTCATGTGGAACA  
AGGCTAAGTGATTAAGGGAGAAAGGGAGAGTCTGAAAACAAGGTTAGGTA  
TTACAATGTCAATAAAATTTGGTCTCTTATACAGTCTTATGGTAGATTTCT  
TTTCCATCTTTAATCTCCCTCTAGCACCACCAGACTTTTTCTCTCTGTAC  
CTTGAGATGTAAATTTTGCTATCTGAATTTTCTGCTAAGAGTTGTTTCTT  
TTAATATGCAAATTTAGGGTTATTTAGCTGACAACCTGCCAAAGTAGTGAA  
ACAAGTTATCAAGAACTTGAACGCTTAAGGTAGGAAAAAAAAAAGTCTTT  
ATGAATCTATAAGATGTACTTCTATTGGCATGCCTAATACGTCTATGTAT  
TTACGTGTTGTGTACACAGTTTTTCACTACTGAAAATATATAGAGGAGTT  
CTAATTAATTGACTTAAGACAATAAAAGCGCTTGAATCAAATACCTTATC  
AGGAAAAAGGAAAAAGACAAGTCAAATGCTTGTTCAGTCTATATACTTA  
AGTAAAACTTTAATAAATAAGCTAGCTTTAACATTATTTGAAATGTCTT  
AAGAATTGCCAGCAGGTTCTGGGTTACAGAATAGTGGGGGTGCAGTGGG  
GTGAGGGTGTGGTGGGGTGGGNGGTNNNACNNNNNNNCCCCCCCCCCCCC  
CCCCCCCCCCCCCTCCCCCCCCCGCCCCGNGCGGGCCGCGCCCCCCCCCGC  
CCCCCGGCCCCCCCCCGCGCCCCCCCCCCCCCCCCCCCCCCCCCCCCCGC  
GCCCCGCCCCCCCCCCCCCGCGCCCCCCCCCCCCCCCCCCCCCCCCCCCCCGC  
CCCCCCCCCCCCCCCCCCCCCACCCCGGCCACACGCACCCCCCCCCCCCCGAC  
GCCCCCGCCCCCCCCCCCCCGCAGCCGACGCCCCCCCCCCCCCGCCCCCG  
CCCCCGACCCCCCGACCCCCCCCCCGCCCCCCCCCCCCCGCCCCCCCCCCCCCG  
GCCCCCCCCCCCCCGCGCGCGCCCCCCCCCCCCCCCCCCCCCCCCCGACCC  
GCGCGCCCCCCCCCCCCCCCCCCCCCGACCCCCCCCCCCCCCGCCCCGACCC  
>Cont1920  
GGCAGTACGCTATAATTCCTCTTACCTTACCTCATCTGTTCTCTGATG  
GATGTACTTTTTTTTTTAGTTTCTAAATTCCTTTTCTTGTCTGGAG  
ATGGGTGATTGATGTAGTCTGGGTATTGTTCCCTCCAAATCTCATGTTG  
AAATGTAATCCCCAGTGTGGAGGTAGGGCCTGGTGGGAGGTGTTTGGAT

FIG. 3 (8 of 52)

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CATGGGGGCGAGATCCC. ATGAATAGC. TGGTACTGTCTCTCAATAG. 4  
AATGAGTTCTCTGAGATATGGTTGTTTAAAGTGTGTGGCACTCCCCCA  
TTGCTCTCTTGTACTGCTTTGACATGTGACATCCCTGCTCCCTTCGC  
TCTCTGCCATGATTGAAAGTTTCTTAAGGCTTCGCCAAAAGCTGAGCAGA  
TGTGGGTGCCATGCTTGTACAGCCTGCAGAACTGTGAGCCAAAATAAACT  
TCATTTCCATATAAATTACCCAGCCTCAGATATTTCTTTATAGCAACATA  
AGAGTGGCTTAATACAGGCTGGGCATGGTGGCTCACGCCTGTAATCCCAG  
CCTGTGGGAGGCTGAGGGGGGTGGAACATGAGGTCAGGAGATTGAGACC  
ACCGGCTAACACGGTGAACTCCATCTCTACTAAAAATACAAAAAATTAG  
TCGGGCGTGGTGGTGGGCGCCTGTAGTCCCAGCTACTCTGGAGGCTGAGG  
CAGGAGAATGGCATGAACCCGGGAAGCGGAGCTTGCACTGAGCCGAGATT  
GCACCACTGCATCCAGCCTGGGCGACAAGAGTGAACTCCATTTAAAAA  
GAAAAACAAAATTTCAAACAGAACAAAATGAAAAAATACCAAGTGAAA  
GGCCCTATAAAAAACCCCTCTGGGGCCCATCTCCCACCCCTCAAGTGA  
AACCACATTTAACAATTTGGTGCATATCTTCCAAACCTTTTGTGTACA  
CATATAAAAAACATACATGCTTTGATTTGGCTCAGACTGTACATAGTGT  
TTCCCTCTTGCAATTTTACACTTAATATATCTTTGACATCTTTCTATGTCA  
GTGCATGTTGGCTCGATGATATTCTATCATTAAATACCCCTTCCAAAAATG  
GTAAATCATTTTAAAAAATCATTACACAAAGTACATATTTACAATTTTA  
AAAGAAAAACAGAAATCCCAAAACACAACGACAAACCTCTAAAAATAATCTC  
TATCTTCCACCAGCATGGAACAGTTCATTCTTTTTTACATAAAACGAA  
TTATGTGATTGGAAAGATTAACCTCTAATCTACACATTTATATACAGAATG  
TTCTATTTGTTAAGCCTATCTGAAAAATAAAAAATTCAGATGATTAATTCA  
CTTACACTTAGAAATTAAGTCAATATACTATGAATACACATTGTGATCAG  
TTATAATATGATGCTTCTTAGTCTAGGGTTTCAATTAATAACAGTAAAA  
AAAATTGGATAAAATAAGACAGCTAATAACTGAAAAATCCAGAAATTCAAA  
GATTATATTGCCAACTAAAACACTGCCATTTACATTTTTTTTTCTACTT  
GGTAGCAAATGCTAATGGAATTCAATCCTGATTACTTAAAGTCAGTTCAC  
ATCACACATTCAATCAGGATAATACGAACATAATATGCCTACTATAGCGT  
TAGATTAAGACATAAAATTTTTTGTCTGAAAGTAATGACTGCGTACCAC  
TTGAGACATTTGTCAACCACTTCAGCACATTGTTTACGAGTGAAGTGGATG  
TCCCAATAGGAATAAAACGACAGCAATATTTCTATCCATACAGATTTTGC  
AAAGCTTCTCTCTTGCAGGTGTCTTAGCTGCTCTTCAGTACTAATCTCT  
TTCTGCAATGAAGTCTGACTTGATTCTGCTTGTGTACTGTCTTTCTGAGC  
CTTCACTGGATCTGCAATCAGAACCTCAAGTGATTTACAGTTGCTCCAG  
ATGTCTGAATTTTTCTCCATTATTTCTTAATGTCTTTGAAACTGAAC  
CCCATTCATATAGCTTCTGTACCATAGGATTATGGAAGATGGTATCAAT  
TTTTCTAGTTAGTGATGGCGTTTTTTTTCAGCAGTTCTTACCAGACACTCCT  
CAAGTGAATGGGATAAATGAATATTGTTTATATATTTTCTGTGCTTCTGT  
TCTAACAGATATTTACACCCTGGATGCCATTAAACATGTTGTCCCAAGGGT  
CTTNTCTGGGCT

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CTTTCTCCCTTTTTACCCCCATTTTCGTAGGGATTGGTTAAAAACCATG  
TAAAAATCCAAACACCGGCGGGGAACGGGGGTCAAGCTCGTATCCCCA  
CCACTTTGGGAACCCAAGGTGGCAGGATTGTGCGAAGCCAGGCATTTGAG  
CCCACCCCTGGGAAAAAAGAGAACCCCATTTTTTTTGAACAAAAACC  
CCAACCCCTCCAGGAAAGAAATAAGTATGGCTGGGTGAAAGTACCAAAG  
ATGGCCGACTGGCTGGTCAAGTAACTTTACCTGATGGTTCGTAGAATATT  
TACCTTCACCCAGGTGGGAGAATTGCTTGAGCCAACCCCTCAGTGTGGATT  
CAGGAACTTGATTTAATTGGTATCGTGATTGTGGATTAGATTCTCAGGGA  
TGCATTCACTAAGTAAAAGTGATAATAGCTACTTTAAGTAAAAATAATGA  
ATGAATCAAAACACTCTAAATCCATGGTGCTATGCTAAGCTCTTTCTGTAT  
TTTATCTCATTTGATATTACAAATATTTGATGTGTTAATAGTAATGACTA  
TCTCCATTTTTTACAAGTAAGGAACTGACATTGAGAGATTAAAAGACTAG  
CACAAATCACAAAGTAAATGAGATTGAATCCGGTCTTGATTCCAAACTC  
TACAGTATTCTAAATTCAAGGAGACTAAATTATAAGATGGAGAGCCAATT  
TTACTTTATAACAGGGTTAGAAATGGCAGAAGAGACCTGACATTCACACCT  
CTAGCCAGTGCATCATCTTCTGTAGGCCAAATATGCAGGAAATCTATAAT  
AAGAACGTCCTTTGGTGAAGGCCAGGTGCAGGGGCTTACACTTGTAAATC  
CAGCACTTTGGGAGGTCAAGGTGGGAGGGTCSCTTGATGACAGGAGTTTG

FIG. 3 (9 of 52)

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AGAACAGCCTGGGCAACAAGTGAGAC...TGTCTCTACAAACAAAAACA  
ACACAAAAACAACCTTCAAGAAAACTCCTTTGGTATGGATCAGAACAGATG  
AATTATCTATCTGATCCAAATGCTTAATGACATTAAGCCACAGTCCACTC  
ACTGCCACAATAGAGATATACCTGCCAATGCCACTCAGGTAATCCCATCA  
AAAGTGGTAATGAGGTCTGCAGCATGACTTGTCTTAGTGATCCAGCCT  
GAGACCTTGAGATTGCAGCATTTTATTCTACATATGCACAAAACATCTGT  
TGAAAAATCTTCTAAATTGATGCAATACATTCTGATCAAGAATACCTGTC  
TGTAATCTCCATAAACCCCTCTCCTTTCTGTTTTAAAAAATAGTAACAGCA  
TTTCTCCTTACATGACAAAGAAATGACTTCACCATCTACGAAATAGTGAA  
TAGGAGCTGTGTGGAAGGAAATTAGCTCTACTTCTTGGTGGAGATGAGAA  
GGGAGTGTTCCTCTGAAAATCAAGGCTCTTGTCTAGTGGAGCCAAAGT  
CGTTTTTTAGAGTGTGGACAGTTGAGAAGATAAGACAGGGACCATCCACT  
CATGTTTTTCTTATTCCATAGGCCTCTCTCAATTGGGCAAAGCACTCCAG  
ACCTTTTGGAAAGAGTGACACCAAGGCAAGCACCTGCTTGGCAGGCCCT  
CAGCTTCTACGCAAGTATAAGTGAGTATATAAAATGGGGTACTTGTGCT  
GTTGAGTACCTTATTTCCAAATGAGGCTGCCGGTGTCCCTGTGGCTGTG  
AGAAGGCTCTACTGGATAGGTGGAAGTTGTGTGTTCTCATCTTTTCTAA  
CCCTGGATTGACTTGCCCAAAAGGAAGCCATTATTAACACTATAATAAAA  
CCATCCTTAATCTGGGACTCTCTTCATGCAGTGGTTCTTAACCAGTGATA  
AACATGAGAGTTACTTTTGGAGCTTAAAAAAATTAAGATGCTCAAGGTCT  
ACCCAAACTGACTGAATCTCCAGAGGTGAGGCCAGGGATGTATACTTTT  
GAGCCAGACCTCAGTTTACCCTGCAGAGCTCATAAGGTTGCATAACCCC  
TTTGTGAGCCACTCTGATGAAAAGAAAAATTGGTGAGGAATAAGTTTAG  
AGAAGAAGGAGCAAAGGTGTTCTTGGCCAGTGAGAGCCAATGACAGGGAA  
ATGCAACAATGTATCCACAAGAAAGGTAAATTACCCTATAGAGCATTTT  
AGGATAAATGAACATCTCATGCCTAGGGTTGAGAGAGGGTACAAAAAAA  
AAAAAAAAAAGACCACTCTGGATACACAACGCGATAAATGGAATAAAGAA  
TTTTTCTCTGTAAATTAAAAAAATCCTTTGTTACTGAGGTATAATTTAA  
TCTATTTTATGTATAGTTCAATGAGGTGTTATAGATAATAAATTTTTTT  
GTAAATTATTATATTGTATATACTCATACTCATTCTTTTAAAGTCAGA  
AATGTATATAACCATTAACCTTATAAATCATTGAGTCATTGAGATATA  
GATACACGAGCATATTTTATATCCACCACAATAATTATTACCATCTCAAC  
AATTCATCACCCTCAAATTTCAAGCGTAGGGGTTTTTAAATGTCAAAG  
GAGTCTACTCAGTGGGAAGAAAGTTAAGGAAAAAACCTTTGGGGCTTTGG  
GCTCCTTCCCCCTGGGGTTAAAAAGGCAGGAAATTGGGCTTACCCCCCT  
GAAATTGGGAACGAAATTTTGGGAAGTTTAAAAA

>Cont: g22

TCAAGCAGCCTTCCTTCCTTGGCTTCCCAAATGTTGGGATTACAGGCAT  
GAGTCAGGATTCCTGGCTTAGTTTACATTTCTAGAGTTTTGTATAAATG  
GAAACATACAGAATGTATTTTTTGGCGAGTGGGGAGTGTCTTATTTCT  
TTTCTTTCCATTTCCCCCCCCNCCCCCGAGACGGAGTCTCGCTCTG  
TCTGTTGCCAGGCTGGAGTGCAGTGGTGGCATCTCGGCTCACCGCAAGC  
TCCACCTCCCGGGTTCAAGCAATTCTCCTGCCTCAGCCTCCTGAGTAGCT  
GGGATTACAGGCGCCCGCCACCACACCTGGCTAATTTTTTTTGTATTTT  
GGTAGAGACGGGGTTTACCATGTTAGCCAGGATGGTCTCGATCTCCTGA  
CCTCGTGATCTGCCCGCTTCGGCCTCCCTAAGTGCTGGGATTACAGGCGT  
GAGCCACCGTGCCCGGCCCAAGTGTCTTATTTCTTAACCAGCTTTCATG  
CAATCTTTTTTATTTTACCATCTCTGTGATCCCACTCCCAAAGGTACTA  
GATGTCGATTGGTCCTTAGGATCAGCTACCATTTGCCCACTGCTTTCCA  
GCCTTCCAAAAATTTTTTCTTTTTTCTTAAAGATACTCCTGTGTGAGG  
CTCAGAACTCTTGAATTGCTACTGCAATATGAACTCGGTGATGTGAATG  
CCAGGGAATTGCCTGATTGATCAAAGAAATGTATCCCTTCTCCCTCACT  
CTTGCTGTCTTCTCATTTGTTTTCCCATCCTTGTGGATTCTGAATTTA  
AATATCCCTTTAATGTTATAATATTTAATGGCGTTTGGCGAAAAGTACA  
GAATTAGGTGCAAGAGTGATAGCTGTTATTTTTTTTTTGGCCTCTGAGA  
CTGTTTATATATGCAAGTTATTTAACAGAAAGTTCTGCAGTGACCTGAGA  
TGTCAGGGGGTCTGATAGAGTACGTTTGAAGGCAGTTACTGGAAAAAA  
TAATGCCATTTCTGGTTTGTACTTCGGTAAGTTCAGATGACCCAATATAT  
TGTTTACATGTGGCATTGAGTAAAAAAGTAGCTTCCCTCCCTTTCTTCT  
TCCTTTTCTCCTTCTCTGCTTCTATAAAGCATCTGCTTTGGGAAACTTCT

FIG. 3 (10 of 52)

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TAGGAGGAGAGCTTGGCAAGCCCGTGGC .ATGGAGAGGTCTTGCAAGAA  
AAAAGAGATGCTCCCACTCAATGCAGGATGGTGTGGAGGTAAATGGGGAT  
ACGTCTGGCATCACTCAGGAATGGGCCTTCCCTGGCAGGGAAAAAAGGGA  
GGGGAAAGAGGAAGGGAATTCNNANATNAATTGCTGAATACGGGGATTCC  
ATGGCCTGGATCCAGGAAGAGAACTTTGGGAGGTGTGAACCTGGAAGGCA  
TCANCTGATGAGGAGCAGCCTGAACTCCGGGGAGGACCTGTTTTTGGTGG  
CCCCGAAAAAATGCCTTCCACACACAGGGAGGCCACCCGGCTGATGGGC  
TGGGGGTGGACGGACAGCCCTAGGACAGGCTTGGGAAACCAGGCTCAGG  
TAGGGCTGCGAGGTTCTCGCTGCGTCTCTTTCCCTCCTGGTCTTAGAAA  
ATAGAAATCCAAGGCCTCTTGAGAGTGGAAAGGTGGGTGGGAGGAGGGCAG  
ATGGGGCTTAGGCCCAGGACACCCGTAGAGCTACTGCCAGCTGTCTCTC  
AGGGACTCTGCTGAGGTCACTCCAAGGATCATTCTTAGCCTTGCTAGACA  
GTACTGACAGAGGGAACCGTAGTATCGCACCCACTTCTTTCTCTTCAAT  
GAAAGTTTTAAAGGTCACCATTTCTCTGGCAAAGGAAGTTCCACAAATAT  
TCCATTTCCGGTCTTAGAAACAGCAAGGTATCAAGCAATTGCAAACTTCC  
TGTGCTGGGGAATCCCAAGGAAGTAGGGGCAGAGTTCTGGTGGAGACAA  
AGTGAATTCGAGTGAATTAGTCAGTAGCAGTAGCAGTAGCAGTAGCAGTA  
GCAGTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGCAGCAGAACC  
AGAATTTCCCGCACGTGTCTCAGGCTCTCATTGCCAACTCAGTCTCTA  
AGTATTTTTATTGGCAGGAAAAATAAAATAGCTATGAGTGAAATAATTCA  
TTAGACCTGAGCCTCCATCAATTTTGTGTTTAAAGGCCTGACTCTCTTTA  
CCTTTCCCTGGGATGGAAGATGCAATGTTCTGATCTCACTGTCAAAAA  
AGAAGAACCAGTGGGTATATTGTATGCTTGAGTCCAGCCATTAGTCACA  
AGACATAGAGATGACTGCCATGTGTGTAGACTTTCTATAGACTGTGTGCT  
AAACCCGACCTGCCACTTCCAAGGAGTAGATGAGGAATGTCCATGGTCT  
GGGGAGCCCTACCCCAATTTGGGGCAGACATTCCAAAGCTCATTTTCTGT  
GGAGGGGGTGGATGGTTAAAGGAACGGCTGGGATTTACTCTTCTTTCTAG  
GGCCAAGAAAAATGACATGCTGCCTCCATGTTTAAATCATCCTTCCCGCTGT  
TAATAACTATGGCTTTAAGTCCCGGTTAGGGCTTCTCCAAAAATTGGG  
GAAAAAAATTCCTTCCCGCTTAAAAATTTTTTTTTTAAAAAACCTTT  
TTTTTGGGGGTGGGAAAAAACCAAAATTTTTTTTCCCGGGGTTT  
TTTAATTTAAATTTCTCCCAAAATTTGTTTTTTTTTCCCGGAAAAA  
AAGACCCCCCAAAAAAAGTTTTTTGGCGGAAAAAATATTTTT  
TTTGTGTTAAGAAATGGAGAAGAAGGGGGTTTTTTTTTCTTCTCCCC  
CACCCGCCAAAGGAAAGTTGTTACAGATTGTTTTGTGTCTCCCGCCCA  
T

>Cont: g23

ATGTGCCTGCGAAATCATCCTTCCAGAAATATTTGCCCTTTCTTTTGT  
ATAGAGTGGCACTGCCCTATATGGTGACCACTTGCCACATGTGGCTGTTG  
AACACTTGAAATTGGCTTGTGAGAATTGCAGTGTAAGTGTAACACAT  
ACCAAATTTCAAAGACATGGCACATAATAAAAAATGTAATAATCTCATT  
AACAATTTTTATATTGACTGTGTAAGTAACATTTTGAATATATTGGATTA  
AATACATGGATGATGCCCCAACACCCACAGTCCCTTATCAAGTCTCTACT  
TCACATTTTTGTACTTCTGACTTAGAAATAGCACTGGCGTCTAAGAGCCT  
ATTAATGTGCTCAATAGGTTCTTGGGAACCACAATTTTAAACAAAATGAC  
ATATAAGAAAACGAATAACATTGAACAAAATGACATTATTCGAGGACCTG  
CTGCATGTTGTTTCACTTAAAGTCAGTGTCCAAGAACTATCAGTGACAT  
TTAGTGAGGAATTGCTGTCTTCTGTTTACAGGAACCTGGGCAAGTTAC  
TTAATTCCTCTAAGCCCGGTTTATATCCCTGCAAAGAGAGAAGGATAATA  
ATCACCAGTACTTAGTGATGTGTAAGGAGAAAAATAAATAAATATG  
AAATGGCTGACAGTGTCTTGTGACACAGAAGATGTGTGATCCACAGTAG  
CTGCTATTGTCTGCCTCACTTCACTAGTAATGGTCCAGGGAGGCCTTTAA  
TGTGCATGGTGCAGTACATTCAATGTTGGACATGGGTGAAGGAAAGAC  
CAGGCTCATCTAAACACAATAGGATGCTTGTGGTGTGTTTGGAGGAATC  
AAGGACTAGTTATCCACAGCTGTAACATGCATGGATCAAAAGAGATAAGG  
CACACAAAAGACTTTGTGAGTAGCAAAGCATTACAAAATGCAGAGACCAG  
CTGTGGGTGGTGGTGAAGTCAAGCCAGCTTCCCTCTGTGCCTGGCTGAGT  
GGTTCTGGGCAAGTCACGCCATCTGTCTTATGATGCCCTTCCCATCTATAG  
AGAGGGAGCAACTGAGGCCCTTCCAATACTGAAGTCTTTATTTCTGCT  
ACTTTAGAAATATCCACATTTTGGTAAATCAAATGATCCAATGATTCC

FIG. 3 (11 of 52)

ATTTCTTAATGTTCAAAAAGAGCCCAACATCTAAATGAATCAAC  
AATAAAATATTTATTGTGTATGTTTTGATTGCTGAAACTTCTATTTTAGC  
AACACACACACACACACAGAACCCATAAGCCTTCATCTTCTTGGAT  
AAACGAGCCTTCTGTCTGGCCATTTAAGTCACGATTAAGTAAATGATT  
CCAACTCGCCTTTTGCAGCAGTTTCAATGGGTCTTCTGCGTGGCAGTG  
GCCCTCCTGACTTATGATTTCTGTGTGTCTGGCCTGTTACCACTGCAGCT  
TAACTGAGGAAACAAGAACAAAACAGCCTCTGACCCCAAGAGACTGTTGG  
AGGCAAAGGCTTCAGTCCCAAGAACCTCACACGTGGGGAGCCCGAGAGCC  
CAGCCCTGACCTTTTCTCCAGTAATAACATAAGAAACAACAGGCACTGGC  
CTTATTTTGGATACAAAGAGTGGTGTCTTCTTAAATCTTCTTTAGTC  
AGGGGTACCCCTTCATGGACGCCCAACATCCATGGTTCCTGCTTGAGTC  
CCTGCTTCCATATTCCTGCACTTCTCACTTGAAATATCCCTGGAGTACGT  
TAAGCAGCCAGGTTTGGAGTTCTTGTGTGTGAGGCGGGTGTGTGCATGT  
CCTCTCTCTCAACAGGACCAAGCTCCCAAAATCAGACGGTATGCCTCCA  
CGCCCTTCCCAAGCCTCCCCAGCAGCACCGAGCATGTGAGGGGAGCTGG  
GGCCAGGCCATGATGGGAAGCACTCTCTGCCTAAAGACTAGGGTGATGC  
GCCCTCAACTGTGGGAATGAGCCCCAGCTCTGGTGTCTGCCTCGTTTTT  
CCTCCTGGACAATCAACATGAACTCCTCACCCTCTTATCCACTTTGCAT  
AAACTGAAAATAACAAACCCAGGGTCTTCTGTACAGGAAAGGGTTTTT  
TTTTATAAGATTAAACAGAGATGATTCAACACACCCAGGATATAACACAT  
GGGCCATGAGTCAAGGCCAGGCATTGCTCTGGTCAGCCTGTTGTTGGGC  
CCCCCTTGGCAGGGCTCTCCCCCTGAATCTTCCCCCTTGTACTCCCCATCA  
CCACAGCAGCTCCAGCTTTGGGTACAAGGCCAGTAAATGGGGAAGGGGT  
CAGATGACATAAAGAGCCCTTCTGTCCCATGAAATATATTTGGATAA  
CAGATGGCAATTTCCCCCTGTGTCTTGGCCAGGGCCAGAGCCTCCACTTG  
CTAGAGGCAGACAGAGGATGGAGAGCCCCCTTATTAGTGGGAGGACATCA  
CAGGTGGGCAAGAAACCACAAGCTTGCCTGAGGCCAGCCTTGAAATAG  
CAGCACCTGCCGGCAGCTGTGGTCTGGGGACAGGGTACAGGATGGAGGG  
GCCTCCTAAGCCTTTTATCTCTATGTACTAAGTACAACCCATTTTCCAC  
CTCACAGAGCCAGATCAGCCTCTGTGAGGTCTGGTGGCAAAAGGATAAT  
TGCCTGCCCGCTGCCCGCGTGGGGTGTGTGTGCTTGCATTCTGGGAA  
GGTTGTTGGGTTACTCTGCAATAGGTCTCTGACCAGCTCACCCTCCTA  
CTGCAACCTCAAACCACTTCAAAGAAGATCCAGCACC

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CGCGTAGTCTAAAGACTGAGTCTGAAGCTGTCCCTTCTGCTATGGACTT  
CAGATTTTAGCCCACTTGAATTGCTCCATATCCTCCAAGCCATGGCCATC  
CCTTGACTCTCTGGGCTCCCAAGCACTTGCTGCCCTTCATCACACAGTTG  
AGTTAAGGCAGAAAGACTGGTTTCCATGTACACTTTGTGGAAGCTTCTC  
ATTTCTTTATATAATCTCTGTCTTTGTCTACTGCTTTAAATCTAGAAA  
TTGTTTACAAACAAAGGTGATCCTTTAAAGCTCAAAGCTGATTGTGT  
CACCATAATATACCACTCTTAATGGCTTCCATTAACTTTGAGTAAAGA  
CTTTATGGAGCCTACATAAGGCCATGACTACCTGGCTCTTATTTTCTCC  
TCATCCTCATCTACCAACTCACTCTCCACTCCTATACCCCTCACTCCTT  
CCCCCTCCTCTCTGAGCTCCAGACTCCCAATTACCTACTTCCACCCTT  
TTTGACCCCCAGGCACTTATCTCAGCCTGGAAATTTCCCTCTTTGCTCTC  
CACTGAACTGTCCACTCCCACTTAAGACATGTGCTTATGTACACGCCCC  
TTACCGTGCTTATCTCAGTTTGTAAATTATCTACTCATTTAGAAAAGTGT  
GATGAAGGCTTCACTGTCAAGCTTTTCAAGATAGCAGGAATCATAGCTGAT  
TTTACTTACTTAACGGGGTTTCACTTCTTTGTAATTTTTTTTTTTTGGAG  
ATGGAGACTCACTCTTGGCCAGGCTGGAGTGCAATGGCATGATCTCGGCT  
CACTGCAACCTCCACCTCCTGGGTCAAGTGATTCTCCTGCTTCAAGCTC  
CCGAGTAGCTGGGATTACAGATGCCTGTCAACACGCCAGCTAATTTTTT  
GTATTTTGTAAAGACGGGGTTTTCATCATGTTGGCCAGGCTGGTCTCGA  
TCTCCTGACCTCAGGCGATCCACCCACCTCAGCCTCCCAAAGTGCTGTGA  
TTACAGGCATGAGCCACGGCACCCAGCCACTCTTTTACTTATGGGTG  
AGAAGCCATTAGAGATCAATTTCTTTCTTTCTCTCTTCACTAAGGCA  
CCAGGGTCACTAAGTAGTAGGATACTTTGAACTAGAACTCAAGAAATTGA  
GTTTTAATTTTACCTCACACTCTCATATGAATCTCCATGTGACCTCGGG  
CCATACTTCCCTGTACCTGTCTTCTTTTATAAAAGTAAGAGTTTAA  
ACTAGATGGTCTCCGACATGCATCCTTCTCTAACATATTCTGGAACCTTC

FIG. 3 (12 of 52)

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AATAAACTAAGATAAAC .GAATAATTAAACTTAATTTAAAAGAACAA  
GGAAAGGAAGCAGTTACATTAAGCAAAAGAGACATCTTCATGGTTGAAGA  
AGTGTATGCCCTGGTGTCTGGATCCCATTTAGGAACTTGGTAACCTTGC  
AATCTTGGGCAGATTGCTTAATTTCTCTAGACCATGACTTCCTCTTCTGT  
AAGATGTGATAAGAACATCTACCTCACAGGTTTCATGAGAGGATTAAATG  
AGATAATGTATTATAATCCCTTGAACATGGTAGGCTGTTATGTTAAGTCC  
TTTCCTCCTTCTCTGTAGCTATCATGGAATTTAAAAACACATTATAACTA  
GAGCATGAGTTGCGACTAAAGGCTCAATTGTCTCTGCATGTGTTGGCTCA  
TGCATGCTTTATTCTCTGAAGAGCTTTTATACCAAGTGAAAGGAAATAA  
TTGCATTTCCCTGAAATTCACAGGAAAAAGTTATGTTTTCTCTTCATT  
CAAGTGATTCTGTTAGACCCAACCACATGCAACAATTTTAAAGTTGCTTC  
CAAATATATTTACAAATATTTCTGTCTTCAAGGAACAATGGCAAGACCA  
TGACTCAGGTTTACATCCGGATTCCACCCTAACCATGTACCCAATTACT  
TCAGTCACCTTCATTGAGGCTTACATATCACAGAATAAAATCAGATTTC  
ATCAGAGGAGGTGAAGACAGGGAGAGGAGATATTTCAATCCCTTCTCCGC  
AACCCCGTTTTTTTTTTTTTTTTTTAAACAAGGATCCTAGAGTTACTGAATG  
ATAGCACGTTTGGGGGAAAGACCCTAAGGATGATCTTTATAAGCCATC  
ACTTGGTGTGGTGGTGATAAAAAACTCGAGTATCTTTATGCACTGGAAA  
GAGAAGATTGGACTCGGAATCAGAAGCTTGAGTTCAAGCACTGGTTTCAT  
CAGTCTTGTGATCTTGGGTTGGTCACTTAACCTCTTCAAGGCTCCTCAGC  
TGTGAAAGAAGATAGTATCAGCTAATTCTTGTATGTGCACTGAGGAGGCA  
GTGAGATAGTGCAGGTAAACTATAAAACAATTGTACATGAAACGCATCA  
CAGTGATTTCTTGGACCCACAAGCTCCAATCTTATAAAACATATCCAGTC  
ACCCACCAACATAGATCATCTCACCTTGCAATCTGATTTTGTGGATCAT  
GGGGAAAAACTGCTGATTCTAGCAAAACCCATGGCATAGGATAAGTGCA  
CAATAATTTTTTTTCTTAAATGATTTAGATGACAGTGACTCATTAAAGGG  
TTTCCTGAGGCCTCCTCAGAGTCGAGAGGTGGGTGCCTGAAGCCACCCAA  
AGTCCCTGTACAGGATGGCTCCCAACGCACACACCACAGGCCTGCCAG  
TATGTTCCACTATCTACCCAGTAGAGCCCTGCCAGTACGTTCCACTGTC  
CCTTCCCTAGAAGAGGTGACTGTTGTTACAGTCCCAGAAAAGCGGGCTC  
CCCAAAACAATGCAAGGACCCACCTCTCTCTGAACCTCACCACCCTAGT  
TTTCCTTTAAAAATCAATTTACAAGAAGATCATGTGAAGGAAAAGGTTGG  
GTGATATTCTAACCCAAGTTAGCTGTTTCTCAACCAAGTTCTCTTTGAAA  
AATTCAACAACCACTTTGGGGAATTATTTACAACAGAGGAGTGAGGATG  
GGACCAGGATAGGTATTGCCTATGTTGGTGGAACCAGGGTTTTTTTCTG  
GATTACCAAAAGAGATGGTATGCATTGCTCCCAGAAGCTAAATATCTTCAG  
GCTTTCAATGGTGGCCTTCACTGAAAATGTTATCCCTGTTGAAGCTTTC  
AAGCCAGTATTTTATAAGAACTATATTTCTTTGGTGAAGTGAAGCATT  
ATAATGATGACTATACAGGTTCTTGAGTGACTGAAGCCATCATTAGCATT  
GTCAATATTTTTGTTTAGTTGCACTCTCCATAGCAGCTCACATTACAATG  
TGCTTTGCAATTTGCTTAGCAATAGCCCTCACAAGATTCTCAGGAGGA  
GAGGGTTAATCCGGATTACATTTCTGTGAAGCCTAGCGAGATTAATCGC

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AAGAGTTTTTAAATTAAGTAAGGACGCCGGGAAACAAATCAATCCCAGCA  
AACATTTTGTGGGATTTATCATTCAAGCAATTTTACAGTTATCCCTGTC  
AAATACATTAAGTGTTCAAAATTGGGCATAGGGGGAACAAAATAATAAAC  
CCAGCCAAAAACAGAATAATCCCTGTTTGTTCATGTTGGATAAAAAAGAC  
ATTACTATTGGTGTAAAGGAAATTAGATACATCTTCCATTATTTAGTAAAA  
TTACCATAACTTCTAACTTTGTGGCTTTAGGCAGTCTAGTCCACAGGCAG  
GAAGGAGGTTTGTGGGCAATGACTGTTATCATCTTCTGTTTCAAAGC  
TAAACCATAAACTAAGTTCCTCCCAAAGTTAATTCAGCATATGCCAGGA  
ATGAACAAGGACAGCCTGGACGTTAGAAGCAAAATGGAGTCAGGTAGGTC  
AGATCTTCTTCACTGTCTCAGTGATGGCAGTTTCATAACTTTAAATGATG  
GCTATCACAGTTTTTATAAATAATCTAGATAAACAGTTAAAAATAAAATAA  
TTAGGTAAATGTAGTGCATAAATATTAGTAGACAACTCACCATAATTT  
AGAATCTAAAGTTAAATTAATAATAATATTTTATTATTTGGTATTTTCC  
AAGAAAAACATATTGTAGGAAACCATTCTTTTTAAAAAAAAGTGTCTT  
TTTTAAAAAGGTGAATAATTTTTGTCTAATTCAAAGTTTATTGAAAAGTTA  
TGTATAAAACAAGGTAAAGGAAACAAGGAAATAAGGGAATGTAAAGAAA

FIG. 3 (13 of 52)

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ATTATAGAAATAAAAGTGGTATTTTTTGGTAAGAAAGCTTAAAGAGAAA  
ATTTTAGGTAAGAAAGAATCTTACCTAAAATTTTGTGCTAGAATAAAGTG  
ACTGGCTAAGAAAGGATGTTCAAAGCTATTTATGACAAACCCACAGCCA  
ATATCATACTGAATGGGCAAAAGCTGGAAACATTCCCTTTGAGAACTGGC  
ACAAGACAAGGATGTCCTCTCTCACCCTCTTATTCAACATAGTATCGGA  
AGTTCTGGCCAGGGCAATCAAGCAAGAGAAAGAAATAAAGGGTATTCAAA  
TAGGAAGAGAGGAAGTCAAATTTTCTCCGTTTGCAGATGCATGATTGCAT  
ATTTAGAAAACCCCATCATTTTCAGCCCCAAAACCTCTTAAGCTGATAAGC  
AACTTCAGCAAAGTCTCAGGATACAAAATCAATGTGCAAAAATCACAGGC  
ATTCCTATACACCAATAATAGACTAACAGAGAGCCAAATCATGAGTGAAC  
TCCCATTACAAATTGCTACAAAGAGAATAAAATACCTGGGAATACAACCT  
ACAATGGACATGAAAGACCTTTTCAGGGTGAAGTGAACCACTGCTCAA  
GGAAATAAGAGAGGAAACAAGCAAATGGAAAAACATTCCATGCTTATGGA  
TAGGAAGAATCAATATCGTGAAAATGGCCATACTGCCCAAGTAATTTATA  
GATTCAATGCTATCCCCATCAAGCTACCATTTGACTTTCTTCACAGAATTA  
GAAAAAATAATAGCCCAAGACAATCCTAAGCAAAAAGAACAAAGCTGGAG  
GCATTGTGCTACCTGACTTCAAACCTATACTACAAGGCTGCAGTAACCAA  
ACAGCATGGTACTGGTACCAAAACAGATATATAGACCAAAAGAACAGAAC  
AGAGGCCTCAGATATAACACCACACATCTACAACCATCTGATCTTTGACA  
AACCTAACAAAAATAAGCAATGGGGAAAAATAATCCCTATTTAATAAATG  
ATGTTGGGAAAACCTGGTTAGCCATATGCTGAAAACCTGAACTGGACCCCT  
TCCTTACAACCTTATACAAAAATCAACTCAAGATGGAATTAAGATTTAAAC  
ATGGCTGGGCATGGTGGCTCAGCCTGTAATCCAGCACTTTGGGAGGCC  
GAGATGGGTGGATCATGAGGTGAGGATGGAGACCATCTGACTAACAC  
AGTGAACCCCTGTCTCTACTAAAAAATACAAAAAATAGCTGGGCATGGT  
GGTGGGCGCCTGTAGTCCAGCTACTTGGGAGGCTGAGGCAGGAGAATGG  
TGTGAACCCAGGAGGTGGAGCTTGCAGGGAGTGGAGATCACGCCACTGCA  
CTCCAGCCTGGGCAACAGAGTAAGACTCCATCTCAAAAAAAAAAAAAAA  
AAAAAAAAAGAAAGGATTTAAACATAAGACCTAAACCATAAAACCATAGAA  
GAAACCTAGGCAATACCATTCAGGACATAGGCATGAGCAAAGACTTCAT  
GATTAGAACACCAAAAGCAATTGCAACAAAAGCCAATTGACAAATGGGAT  
CTAATTTAACTGAAGAGCTTCTGCACAGCAAAAGAACTATTGTGAGAGT  
GAACAGGCAACCTACAGAAATAGGAGAAAATTTTTCAATCTATCCATCTG  
ACAAAGGGCTAATATCCAGAACTTACAAGGAATTTAAACAAATTTGCAAG  
AAAAAAAAAACCCATCAA: AAGTGGGCAAAAGATATGAACAGACACATCTC  
AGAAGAAGACATTTATGTGGCCAACAAACATGAAAAAAGCTCATCATCA  
CTGGTCATTAGAGAAATGCAAAATGAAACCACAATGAGATACCATCTCAT  
GCCAGTTAGAATGGCGATTATTAAGAGTCAAGGAAACAACAGATGCTGGA  
GAGGATGTGGAGAAATAGGAATGCTTTTACACTGTTGGTGGGAGTGTGAG  
TTAGTTCAACCATTTGTGGAAGACAGTGTGGCAATTCCTCAAGGATCTGGA  
ACCAGAAATACCATTTGACCCAGCAATCCATTACTGGGTATATACCTAA  
AGGATTAGAAATCATTCTATTGTAAAGACACATGCACATGTATGTTTATT  
GCAGCACTATTCACAATAGCAAAGACTTGGGAACAACCTAATGCCACC  
AATGATAGACTGTGTAAGAAATGTGGACGTATACCCCATGGAATACTAT  
GCAGCCATAAAAAAGAATGAGTTCATTCTTTGCACGGAAGTGGATGAAG  
CTGGAAGCCATCATTCTCAGCAAACTAACACAGGAACAGAAAACCAACA  
CTGCATGTTCTCACTCATAAGTGGGAGTTGAACAATGAGAACACATGGAC  
ACAGGGAGGGGAATGTACACACCAGGGCCTGTGAGGAGGTGGGGGGCAA  
GGGAGGGGATAACATTAGGAAAAATACCTAATATAGATGACGGGTAAATG  
GGTGCAGCAAAACCACCATGGCACATGTACACCTACGTAATAAACCTCCAT  
GTTCTTCACATGTATCCAGAACGTAAAGTAAATTTAAAAAGAAAGAA  
AGAAAGAAAAGGATGTTACGACAAACCAGAAAGTCCAAGCATGTCATGA  
ATAGTCTGTGTAAGTCACAATAAGAGGATTTATTTAAAAAACTTTTATA  
TGATAAAGTTGTCTATAAATTAAAGGGAAATTATAATGGTCTTTCTAGAGA  
TTGGGTTGATGTTAAAAAACTACTTATATATTAATAAAATTTGGTTAGAACA  
ATGAAATTTTCTTACGGGGTTGATTCACTCTTAATAAATTATAAGAGACT  
TAAGAATTTTTTTTAAACCAAAGTTTCAAGCTTTTATTGCATCTTGCTGTT  
TTAGGTTTTCTCTCCCTTTTAAAGGGTGGGAAATAGTAATGCCCTCCTT  
CAACTCCCTTCAGCTCATATACGTTTTTACCCTCAGATTCTGTTTGTG  
TGTCCTGATGCTAACAAATGTTTTCTTAAAGGTCTAAAGGAAATGTTTTCT

FIG. 3 (14 of 52)

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TCCAACATAATATTCTG1GCATTGCAGAAGGTCTTTTCTTTTGCCCTTTT  
GTAACCTGGCTTAACAGATTTTATGTTTTATTGAAATAATTTCTATGCCAT  
TATTATTAAGTTTTGGTTTGCTTAGAAAACACTGAGATTAATACAATTTT  
TTAAAAATTATGATTATTACATCCATATATCTTTATGTATGTGCTTTTAA  
AGTCCTTGTGACATTGAGTTCTAGGGCTTGACTCCTGGGTCTTAAAAGGA  
CAAGTCCTGCTAAATCTTAAATACTGACAGCAATTAAAGGCTCATCTTCA  
GGACTGGTAGAAAATGCCAATCAAAATAAACTGCATTCTTGAAACACAGA  
GCCAGAAAATTAAAGCTATTCAACTCAAGGCCCAGGAACTATAGTGGAAGA  
GGTGGGTGTGTGAGATTGTAAGGGCCAATTTTGAGAGATAAAATAAGTTC  
AATTTCTCTATAAAATTAATCATAATCATTGATGTCCAAGCCACACTGATG  
CAAGATCAGCATATGGGTCTGTGTGAGATTAAACAGGTTTTCTTGAAGC  
ATTAACCTACTCCTTAATAAAGGTTATAGAGGTTATAAAAGGCTTCTGGA  
AGTTATAGCTATGGTCAAGATAAAAAATTTTCATAGATTGTTAATACAATTT  
TGGAAAACAAATTTAATTGGCTTCTTGCTGTTTTTATTAGGGCTTATTGT  
TTGGAAAATTAAGTCTCGTCTCTCAAAGAATGAAGGCTTTTACCTTTTTT  
TTTTTTTTTTTTTAATCCTTGAGTTATCACTTTGGTCAAATGAATGACTTA  
TTTTACAATGACCTTTTCATCAAGTGTTTTAAACCTTTCAAATTTGACAAA  
CTTTCCAAAATCAAACCTACAAATTATGTCTTTTTATGACCTAATGAATCC  
TTTAAATACTAGGTTCCCTAAAGTCCAAAAAATAAATAACATAA  
TGTGGCTTATTTGGTATAAAAAATTTTACAAGAAACATTGTCAAATATAAA  
ATATTGTGTGGTTTTGTTTGGGCTGTATTTGTATAAATATGTTATPGGTA  
TGTGTTCCAAAATTATAGGAACTCCTATAATTCTGATATGACTTGGTGT  
ACATTATCAGTAATAATTATAATTGTTATGGTAAATATTGTGTGCCATG  
GAGGTAACAAATTTCTCATCAAGTGTGTCTTTGACTATGGTTGCCCTAA  
AACTTTTTGCCATTACAGACAATTGTCTTGCTTTGGTCTCTTTAGAAG  
GTGGTTTTATAATCAGCTATAAACTCTAACGGGTGCTCTTGAATGCAGG  
CTTAAGATAGCTTTGGAGACTGTGACATCAGAATAGAGGAAAACTTTCA  
GTATTCATGGAGTGCTGAAATATTCTGAATATCAAGCAAAACAGGAATT  
AACTTCATAGATGGAACATAAAGAATGCTGAAGTAATCTTTTTGACTTTT  
TTTCTTAGAATGTTGATCCTTCGTTTTGTTTTTTCAGAGTCNAGGAAATTT  
TTCTGTTGAGATATTGACAGCTTTAACAATTAAGTATACTCCAGTGAACA  
CAATTTGGAGCA

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ATCTAGTCATTCCCCAGCCTGACCAATTCAATGGCCCCCATCTTAGTTAA  
AATTCCTCACCCTGACAAGGCCCCCATCTACGCCTCTGACCTCATGCCCTC  
CACTCTCAGTCTTGCACTCACCCCTGCCACACTCAAGGGCTTCCCCAGGTT  
CCTTCTTAGATTCCACCGATAGCTCAGGGACTTTGCACATGCTACGGTCT  
CTGCCTGGCTCCTCCCCAGATCTTCTCATGCCTAGCTGCTTCTCATCAGC  
ACCCCTCAGAGACTGTCCCTGCCCCACCTCTCCAGGTTCCATACCTGCCA  
CCCTCCCCCAATCACGTAACAGTTTCTTACAGAGCGAGTTACCATCCCA  
GTATTTCCCTAACTTATTTTTGTGACTGGTCTGTTGCCTGTCTCCACCA  
CAAGAACATAAGCTGCATGTGAACAGGAGCCTTGTCTATCTTGTCACCCC  
AGTGGCTGTGACATAACCTGATACACATTAGATGCTCAATGATGTTTGTAT  
GAATGAAGTGCTGGTAGTCCAACCTGTGTTTTCTTGTCTGTGTAAGTATGT  
CTGTTGTGGTTTTCTAAGAACCCTACAGCTCTCCCACTGTGACTCCTGTTT  
TATGGTCTCTGATTGTGCTGGACTAGAATCCTAACCTACATGCTTACTCTTA  
GTGTCTCCCCCAGAGGCTGAATCCAGTCCCTAAACCTCCACCAAATGG  
CTAAGACCTAGCTTCCAACCAGACAGGCCTACGCTGAGACCTCAGCACCG  
CCCTTCTGCGGTCTCATCTTAAACGCATCCTTCAGGGCCCAGCTTAAATG  
TCTCTTCTCCAAGGAAGGCTATCCTCTTTCTGCCCTCAGTGCTCTCCAT  
GCCTCCTCTATGCCTCCATGCCTGCTTTCAACCCCTGCAGAAGTGGAGAAA  
TTGCTAATCTGCTGTGTTGACACTGTGCTGGGGTGCTTGGGCCAGGGAG  
CAGGCTGGTGGTGTGCTGATAGCCCGTGGCTGTGCCCAGGTCCATGCTCA  
CTTCTGAGCCCCAGTGGAGTAGGCTCCCTTTCCCTTATTGCAGCACTCA  
GAGGAAGGACGTGCTTCTTAGGACAGATCTGGCCAACCTCTCCCTCGTGA  
GAGAAGGCCCAGCCATCCTCTTGCCCTCTTCTTCTCCTGCCCCGAGT  
AATAAAGGTGCCTGGTCAGAGCCTTCTAGAAGGAGACCCAAACATCCACC  
ACACATTCAGGTTCCAACCGTCAATCCACATGGCTGGCTGTGCAGGTAAA  
CGCAGAGTCTGTTTACACACCCCAACCATCTAGTATTGGATGGGAGGACA  
GTAGCGTGACACTCTTCTCCAGCCTTGAGCCCTACTGTGGGCCCCACCCA

FIG. 3 (15 of 52)

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ACCCAGATACCAGAGGAGCCCTGTAAGGATGCTATTGGATGCTTGGCC  
AGTCATGTACAAAGTTAGCCCTTTGTTATATAGAGTTAGCTACGTACATC  
TTCCTCTGTAGGGAACCCAAGAGGGGAGAAGAGATATGTAGTAGGATTTA  
ACCTGCAAATCCTCTGCTGAGCACCTGCACTACATACAGTGGGTAGCAT  
GTGGTAGGTGCTCAATAACTATTGACCGATAGATTGAATACAGGTAGGAT  
GGTGACACAATCTAAGATCCCAGGGGTGGGGAGACCACACGCTTGGTTAG  
GGAGACCCAAAGTGGACCGTGTGGCCAGAAGAGTCCCGCACTGCACTCTA  
GTGACAGTGCAGAAAGTCACTGTGGGAAATCTAGAAGTTTCTACAGGTTG  
CTATTTTCATCATAGCACTGTGCAGGCCAACCTTCTGCTCCACTGGCTG  
TTGGGAAAAGCTTTCTCTTTTCTTCTAGCCAGGGAGCTCTCAAAGTGT  
CCACTCTCTCACCTCCACCCAGGCGTCCAGGTGTGGAGGACACTTGCCTG  
CTGCTTGTCTGCTGACTCATCCCTTGGTTTCACTTGGAAAACCTACCACC  
AGCTGGCCTCTTTCCAAGCATCAGCCTCCTCATTTTCTTAATCCCTTAGG  
TGTGATCTCACCTCCACACAGTAGATTGCCTCAAGGCCAATTCCAATAT  
GAATAAAAATGATTATTTTGTCTCTTCCAATCTTCTTTTAAATATTA  
TTTTATAATTCCCTTTAGGAGGATCACCTAAGTGAAGACTATTTTACCT  
AAGAAATGTTAAATGTAAAGACATGGTTGTAATCTGGGGATTCTGTTA  
AAATGGCTAGCAGACAGAAGTCAGACGACAGGCTAGAAATGTGTGAAGAG  
TGGTTGGCTTTGAAAGGCGAGTTGGTAATGATTTTCTTCCATTTTCCA  
TGCTTTCCAATTCTCTACAAAGGCCTTAATATTACTTCGATAACCAGGAC  
CTCTGATAACCTGCCCCACCGAGTAAAGACTTAGCTGGGAAAGTCAGCT  
TCATGTGAGGTAAAAGGAACCGAGTAATACACAATCCCACTGCCAAGT  
TCGGGTGTGCGAGGCTGAGCTTCTGCTGTGGGAGGAAAGAGAAAGAAG  
AGAGAACTCCAAGATCCAAGAGATCCAGCAAGAAGGCTGGAGTCTGAGG  
ACGCAGAAAGCTGAATGGCACAGTTACCCTATTGTGCTGAGGTTCTGTG  
GCCTCTGGGTCTCTTGACAAGTGGGCAAAGACCCACAGAAAATATCTCT  
AGACCTACCTGTGGGAGGGGAAAGTGCTTAAGATCATTTACAGGACAGC  
CACCTGGACCTCAAATGGCTTACAGTTCCTTCATCCAGAGGCTCTTCATT  
TAGTACATACCAGGTGCTAAGCTGGGTGCTGGAGACATGACGGGGAACCC  
ATTTACCATGGCTTTGTTACTGTGACATTACATCTAGGGAAAGCCAGCA  
AAGGGGAGGGATCGAGGAGAGCTTGTAGGCAGAGAAAATACCCAAGGGC  
AAGGGAGAAGCCAGCCTGTTCTGAGCACACACAGTGGTTCCATCTAAGT  
GGCCTCAGTGCCAGGTTGGACTGGAGATGGGGCTGAGGAGCTGTACAGA  
GCATTCTGGACACAGATGTACATAGTCCCTTGAGGTTAGGGTCTTAGG  
CATGGCAGCATTGCTTTGAGTTTTTCTTTTGTAAATGTTGCCATTCTGA  
CAATGTGGAAGATGGGTCTTGACAGAGAAGGGCAGGGCTGTGAGACCAGT  
TAGGAGACTAAGATGTGAGCCAAGGAAAATGAGGAACACCTGAACACTGG  
GGCAGGTGACAGGCCCAGAGAGAAGCAGATGGCTTCTGAGGTTTAAAGT  
AGGTAGAATCAAGGCAGCTGGTACAGATCTTTTATTACATATAAACTGGA  
ATAAGCCATCTGTTCCAAGACAAAAGAGTAGGCGGAAAACAATACAAGAC  
AGAAATGGAATTAGAACAAACCTGGGAGGAATGTGGAATTAGAGTAGAGA  
GTCCAACACTGGCTGCAATCATAAAAATGTAAACAAACAAAAATTTGCT  
AGGTGTGCTTACTTAGAAATAATTAGCTGTCTATTAAGTTCACTGTGT  
TATGGCTTAAATGTGTCCCCCAAAATGTGATGTGTTGGAACTTGATCCC  
CAATGCAACAGAGTTGAGAGATGGGACCTTTAAAGGTGATTAGGTGATA  
AGGGTTCTGCCCTCATAAATGAATTAATACTGTATCATGAGAGTAGATT  
CCTGATAAAAGGATGATCTCTGCCTCCTCCCCACAGCCCTCTGTGCATG  
CTTTCTGCCTTTCCACCTTCTGCTATGGGATGACACAGCAAGAAGGCCC  
TCACCAAATGCAGCTCCTTGATCTTGGACTTTCCAGCCTCCAAAATGTA  
AGCCAAACAAATTTCTGTTTATTATAAAATTACCCAGTCTCAGGTATTCTG  
TTCTAGAAACACAAAATGGACTAAGATCATTAATATCATTTTTTATCA  
GACTGTTGA

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AAAATATAACAGAGAGTAAGAGGAAAATTACCTTCTTTCTTTTCTTTT  
CCTGCCTGACCTTATTACCTCCCATCCCAGAGCATCCATTTATTCCATT  
GATCTTTACTGACATCTATTATCTGACCTACACAATACTAGACATTAGGA  
CAATGTGGCCTGCCTCCAAGAACTCAAATAAGCCAAGTGAATCAGAGA  
GGATTAATCACCTGCCAATGGGCACAAAGCAAGCTGGGAGCCAAGTC  
CCAAAATGGGGCTGCTGCTTCCAGTTCCTCTCTGCAATTGATGTCA  
GCATTATCTTCTGCTCCAGTCTGTCTCCACTACCACTTTCCCCCTCAA

FIG. 3 (16 of 52)

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CACACACACACACAACAGCCTTAGATGTTTTCTCCACTGATAAGTAGGTG  
ACTCAATTTGTAAGTATATAATCCAAGACCTTCTATTCCCAAGTAGAATT  
TATGTGCTGCTGTGCTTTTCTACCTGGATCAAGTGATGTCTACAGAGT  
AGGGCAGTAGCTTCATTTCATGAACCTATTCAACAAGCATTATTCACTGAG  
AGCCTTGTATTTTTCAGGCATAGTGCCAACAGCAGTGTGGACAGTGGTGC  
ATCAAAGCCTCTAGTCTCATAGAACCTTAGTCTTCTGGAGGATATGGAAAA  
CAGACAACCCCAACCAACCAAAAGAGCAAGATGCTGCAAAAAAAAAAAAA  
AAATGAATAGGGTGCTAAGATAGAGAAAAGTGGGAGAGTGCTATTTAGAC  
AAAGTGGTAAAAACAAAGCCCTTGTGAGATGAGAGCTGCCGACAGGAGG  
GGGCGGGTTCATGGTTGTGGGTTTTTGGGTAGGACATTTCAGAGGAGGGGGC  
GGGTCTGGTTGTGGGTTTTTGGGTAGGACATTTCAGAGGAGGGGGCGGGT  
CGTGGTTGTGGGTTTTTGGGTAGGACATTTCAGAGGAGGGGGCGGGTCTGT  
GTTGTGGGTTTTTGGGACATTCAAAGAGTCTGAATGCACCCAGGCCTAC  
AACTTCAAGATGGTAAAGGACAGCTCCAAGGATCAGAAGAAGCATGCTTG  
GAACTGGGGCATTTTGAGAAGGAGGAAAAATATGCAGAGACTAGTGCTTG  
CAGAGCTTGCATGTGGATTTTCATTTGAGGTACAATGAAAACCCATTAAATG  
GGTTTTACACAGTGCAATGGCCTGACCTCACTTATATTTTCTTAAATAGA  
AAACAGATCAGAAGGAAGGCAATAGAGAAGCAGAAAGTCCAATGAGGAGG  
TTTTCACAGCAGTCTAGGGGTGGGGTAAGGAAAAAGAGTGAAAGAAACA  
GACAGAATTGGGTTATATTTTGGAGATAGAACCAACAGAAGGAAGAGGAG  
AAACAACATTTACTGAGAAGGGAAAAAGTAGGAGAGGAATAGGTTTGGGA  
AATAAATCCTGCTGACATTGGAAACCCCAAGGAAGCCTCAAAAGTATATT  
TACTTGTCTTAGATTTAAAAGAAATAGGAAAGAAGCATCTCAACTTGAAT  
TTGAAATCTATTTTCCATAAAAGTATTGTTAAATCTACTCATACTCAC  
AAGAAAAGTACATTCTAAAGAGTATATTGAAAGAGTTTACTGATATACTT  
AGGAATTTTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTAAAC  
CTTCAATTGTTGACTTAAATACTGAGATAAATGTCATCTAAATGCTAAAT  
TGATTTCCCAAAGGTATGATTTGTTCACTTGGAGATCAAAATGTTTAGGG  
GGCTTAGAATCACTGTAGTGCTCAGATTTGATGCAAAATGTCTTAGGCCT  
ATGTTGAAGGCAGGACAGAAACAATGTTTCCCTCCTACCTGCCTGGATAC  
AGTAAGATACTAGTGTCACTGACAATCTTCATAACTAATTTAGATCTCTC  
TCCAATCAACTAAGGAAATCAACTCTTATTAATAGACTGGGCCACACATC  
TACTAGGCATGTAATAAATGCTTGTGAATGAACAAATGAATGAAGAGCC  
TATAGCATCATGTTACAGCCATAGTCCTAAAGTGCTGTTTTCTCATGAAGG  
CCAAATGCTAAGGGATTGAGCTTCAGTCCTTTTTCTAACATCTTGTCTC  
TAACAGAATTCCTTCTTTTCTTCATAGGAGATGCCTGAGATACCCAAAA  
CCATCACAGGTAGTGAGACCAACCTCCTCTTCTTCTGGGAAACTCACGGC  
ACTAAGAACTATTTACATCAGTTGCCATCCAACTTGTTTATTGCCAC  
AAAGCAAGACTACTGGGTGTGCTTGGCAGGGGGGCCACCTCTATCACTG  
ACTTTCAGATACTGGAAAACCAAGCGTAGGTCTGGAGTCTCACTTGCTC  
ACTTGTGCAGTGTTGACAGTTCAATGTACCATGTACATGAAGAAGCTAA  
ATCCTTTACTGTTAGTCAATTTGCTGAGCATGTANTGAGCCTGTAAATCT  
AAATGAATGTTTACACTCTTTGTAAGAGTGGAACCAACTAACATATAA  
TGTGTATTTTAAAGAACCCCTATATTTTGCATAGTACCAATCATTTTA  
ATTATTATTCTTCATAACAATTTTAGGAGGACCAGAGCTACTGACTATGG  
CTACCAAAAAGACTCTACCCATATTACAGATGGGCAAAATTAAGGCATAAG  
AAAAC TAAGAAATATGCACAATAGCAGTTGAAACAAGAAGCCACAGACCT  
AGGATTTTCATGATTTTCAATTCAGTGTGCTTCTACTTTTAAAGTTGCT  
GATGAACCTTAAATCAAATAGCATAAGTTTCTGGACCTCAGTTTTATCA  
TTTTCAAAATGGAGGGAATAATACCTAAGCCTTCTGCCGCAACAGTTTT  
TTATGCTAATCAGGGAGGTCAATTTGGTAAATACTTCTTGAAGCCGAGC  
CTCAAGATGAAGGCAAGCACGAAATGTTATTTTAAATTATTATTATA  
TATGATTTATAAATATATTTAAGATAATTATAATATACTATATTTATGG  
GAACCCCTTCATCCTCTGAGTGTGACCAGGCATCCTCCACAATAGCAGAC  
AGTGTCTCTGGGATAAGTAAGTTTGATTTCAATTAACAGGGCATTTTG  
GTCCAAGTTGTGCTTATCCCATAGCCAGGAACTCTGCATTCTAGTACTT  
GGGAGACCTGTAAATCATATAAATGTACATTAATTACCTTGAGCCAGT  
AATTGGTCCGATCTTTGACTCTTTGCCATTAACTTACCTGGGCATTCT  
TGTTTCATTCAATTCACCTGCAATCAAGTCCTACAAGCTAAAAATTAGAT  
GAACTCAACTTTGACAACCATGAGACCACTGTTATCAAACTTTCTTTTC

FIG. 3 (17 of 52)

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TGGAATGTAATCAATG1 . TCTTCTAGGTTCTAAAAATTGTGATCAGACLA  
TAATGTTACATTATTATCAACAATAGTGTGATAGAGTGTATCAGTCA  
TAACTAAATAAAGCTTGCAACAAAATTCTCTGACACATAGTTATTCATTG  
CCTTAATCATTATTTTACTGCGATGGTAATTAGGGACAAATGGTAAATGTT  
TACATAAATAATTGTATTTAGTGTACTTTATAAAATCAAACCAAGATTT  
TATATTTTCTCTCTTTGTTAGCTGCCAGTATGCATAAATGGCATT  
AGAATGATAATTTTCCGGGTTCACTTAAAGCTCACATTACACATACACA  
AAACATGTGTTCCCATCTTTATACAAACTCACACATACAGAGCTACATTA  
AAAACAATAATAGGCCAGGCACGGTGGCTCAGACCTGTAATCCCAGCAC  
TTTGGGAGGCCAAGGTGGGAAGATCACTTGAGGTCAGGAGTTCAAGACCA  
GCCTAGGCAACATAGTGAGATCTCATCTCTACAAAAAATGAAAAAT  
TAAAAATGAGCTGGACATGGTAGTACACACCTGTAGTCCCAGCTACTCG  
GGAGGCTTGAGGTGGGAGGATCACTTGAGCCTGGGAGATGGAGGCTGCAG  
TGAGCCATAATCACACCATTGCACCCCAACCTGGGCAACAGAGTGAGACC  
CAGTCTCAAAAGATAAAATTTTAAAAATGTTAAAAATATATAAAAGAGA  
ATTTTAAAGAAACAATAATAGATCAAAGCATGGATGCAAGATATATTTA  
GTTGGAAAATCAAGGTTAAATCAAGGGATCTTGAATTAGGTGTGGTAG  
ATTTGGGTAAGGAGTAGTCTAAGATGACCCTGTTTCTTGGTACTGGAGAC  
TGGATGAGTGGCAGCGTCTTAACCATATTTTGGTAGAAATATGGAGGTC  
TTCTCCATTCCAGGATGAATGATGAGTAAATTTTAGGCATGTAATTTGA  
GCTACTAGAAGGACACTCAATTGCAGATGTACAATGGGGAGATGATAACC  
TATCTGGAACTCAGAAAAATACTGTATATAGATATGAAAGACATCAGTA  
GGTATGTAGTAGATAAAATCCTAAAGTGATGTCAAAGGGAGAAGAGAAG  
TATATGGTGAACACTGTTGTTTGTCCATGCAATTGCCATCTCTTCTCTT  
CCTTACTGACAGAACCCTGATTTCACTGAGAAGTCAACATGCCCTTCCCC  
AATTGATGAATCCAATTGGTTGAAGATTATGTTCAATTCTATTCTTACATG  
ACTAAGTCACGTTGACTTAATCCTATCAAATGAGATGTGATCTGGAAAC  
AACTTCTGGAAAAGATTTTCTACCTTGATAAAATAAAGAGCCATATAGAT  
GGTCTTTTATCTTCTTCTTCTTGAATGAGATATGTTCTATGAGGAAGT  
GAAGCTTAGAACTGTGGTCAGCAACTTGCAACGACTGGGAAGTCAGAGCC  
ACACAATGAAGAATGCAGAGTGGGAAGGAGAAAAAGAGCCAGCATCTCTGA  
CAACATTGTTACACCGAGAACCCTACCTCCAGATTTTAAGAAAACAAGAAA  
TGCTACTGTTATTAAGCCATTTCACTGGGTTTGCTATGACTTGCAGTCAA  
ATCTAGCTTAACTGATACAGAGCACCACAGAGAACTGGTCTCTCATTTGT  
CTCATCTGTTCTTCTTAGCAGCCACGACTTCTTAGGGTTTCTTAGCC  
CAAGTCTGGCTAGAGCAAGACTAAGTAAGACTTGATTCTTAAATGTCCTT  
TTGTTTTAAGAAATATTAAAGAATTATTTTTATATTAATATATTTAAGA  
AATAAGGAAATACAAAACACTGAGCAAGCAACACAAATCAAGAAATCTT  
AAAAAGTATAATAGCTGCTCAGTCTCTGATTACAGTGAAATATGGAATC  
ATTGTAGAAATGGCCTTGAGCGTTATTCTCCAGGCCAGCTATCCTTAT  
GGTCTGCCCCACCTCCCTCATTGCCTAAACAGTAAGAGAGTCCCATGGTG  
AGACTCAACAGTCTTAGCACAGAACTTGTTACAGTCTATTTCTTTCTTA  
CAGTCTATATATCAATTCAAATCAATGAGAGTAAAGCCCAATCCCTGC  
CTTTAAACCCAAAGGACAGAAGCCCAAAGCCCAAAGATATTCCTAACCT  
TCTCCCCCT

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CCTGTGCTCCCTATGTTTAAAGCTGGGGATCTCTTTTTCTGTGTCTAA  
TTATTTTCTCATTTGGCTTGAAAAATCTGATAAAACATTTTAGGACTGTG  
TATAAAATAGAATTAGCCAAGTGAATGTCTTTATTCAGAAGAAATTTCA  
TGGACGTTGTGCCTACTCTCTGGCTTCTGGCTTCATGGCTTTCAGAT  
CCCAAGTAAGCTCTGGATAGTAGAAGTTATAGTAAGACTGACTTCTAAA  
TAAATGAAGTGACTTAACTTACTGATATGGCTTAAAGAAAAGGAGTGG  
CCTTTAAGATCCATGAACCTTCTCAAACAAAAGTGATAACGTTATCTCCAT  
GCATATATAATACTAAATATAATGCAACTGAGAGAAGTAGGCTGTGGTAA  
GAAAGGAGACCCAAGTGCCATCTGAAGGCAGCACTTACCACTCTGCTTCA  
TCCCACCGAGGAAACAAAGCATGAGTATTGCCAGATTTTCTTCTGTTTCA  
AGAAAAGCCAGAAATCCAGGTTTTTGGGTGAAATGTCTGATTTTAAATGT  
TGGGAACATAATTTATATTTTGAATAACATTGTGTGGGACAAGTGAACCT  
GTATGTGGAACGCTTCTCCAGTGGCGACAGTTTGGACCGTTGATAC  
TCAGCAAGTTTCAAGCAAGTGCGCTTGTCAATTGTGATCATCAAGGTGAT

FIG. 3 (18 of 52)

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BTGTGATTGGTCAAACAATTAGTTTTGCTCAGCATCTCGTGTGTTTTCAA  
AGGACCTGAGGGTTTCATTTGCCCATGCAGATCTTGTAGTCCTGTTTATTC  
TATTAATTTATCTTGCAAATCTATAATGTTTTATTTAAGCAGCGAGAGC  
CGTGGCAGCCTTTGGTCTGGACCCTTTCTAATGATCATTTAGTATCAGGC  
TATGTGGGAGTTGATTGTTTTGCATTGCCTGAAAGCCAACAGTATCACTC  
CTCCTCTAGGTGTGGCAGAGATGTGAGAGAGGGAGACTGACAGTCTGTGG  
GTGTGTATGCAGTGTGGGGGAAGCGAGGCACAGGGGACAATACTGTGGT  
GTATAAAACTAGTCTAAGGTAGCATCAGGAAGTTCATGAAGCCAAAATGA  
TTTTTCATAACAGCACAAGACATTATTTGTTTTTGCCTCCCTCTCATTTTT  
TTTTTTTTTTGAGACAGAGTCTTGCTCTGTCTCATCCATGCTCGTGTGCAGT  
GGTGCAATCTCGGCTCACTGCAACCTCCACCTCCAGGGTCAAGCAATTC  
TCATGCCCTCAGCCTCCTGAGTAGCTGATTACAGGTCTGCACCACCCCGCC  
GGCTAGTTTTTGTATTTTTAGTAGAGATGGGGTTTTGTAATGTTGGCCAG  
GCTGCCCTGTCATTTTTTTTTACTAGTGTCCAGTGGAGTTTTTTAGGGG  
CTACATAACATGATACTGTCTAATCTAATGGCTAATGAAAGGGATATG  
TATATGTTTTTGTGTTTTAAACAAACTTCTTTGGGGTCTCAATAATTTT  
TAAGAGTATAAAGGGGTCTGAGATCAAAGAGTTTGAGTCTGTCTGGACT  
GGGACAGTGGTTGTCAACCCAGATTGTACATTAGGGTCACTCTGGGAAGCT  
TTAAATAGTACTGATGCCCAACCTTACCGCAAACCAATTAAGCCAGAAT  
CTCTGTGGATGAGAAGTCTTCATTGTCTCATCACCATGACCATCATCAT  
GTGCACCGTCACTACACCATTATCATCATCATCATATCATCTTCATTATC  
ATTGTTAGTATCTCCATCACCATCATCAGCATCACCATTATTATCATCAT  
CATCATCCCCACCATCATCTCATCGGAACCTCACCTGCATGGAGGACAA  
TCCACTATGCATTAGGTGCTATGCTATTTGCTATACTCCTTATTCTACA  
ACTGCCCAGAGAGGCTGATATTATCTCACTTTATAACAGGAGGAATCTGG  
ATCGGAAAAGTTAAGGTAAGCTAATTCACAGAGCGAGAAGAGATAGAGCC  
AGGATTCGAAACCAAGTCTCTGTCTACATCAATGTTCCAGTCTCTGCACT  
ATTGAGAACCTCTTTAGTTATGCTTTCAACCCCTCCAACACCACAGTAAAT  
TTTTCTTTTTTAAAAAAATTATACTTTAAGTTATAGGGTATATGTGCA  
TAATGTGCAGGTTTGTACATATGTATACATGTGCCATGTTGGTGTGCTG  
CACTCATTAACTCGTCATTTACATTAGGTATATCTTCTAATGCTATCCCT  
CCCCGCTCTCCCCACCCCATGACAGGCCCTGGTGTGTGATGTTCCCCACC  
CTGTGTCCAAGTGTCTCATTTGTTCAAGTCCACCTATGAGTGAGAACAT  
GTGGTGTGTTGGTTTTCTGTCTTGTGATAGTTTGCTCAGAATGATGGTTT  
CCAGCTTCATCCACGTCCCTACAAAGGATATGAACTCATCCTTTTTTATG  
GCTGCATAGTATTCCATGGTGTATGTGTGCCACATTTTCTTAATCCAGTC  
TATCATTCGCTGGACATTTGGGTTGGTTCCAAGTCTTTGCTATTGTGAATA  
GTGCCACAGTGAACATTCATGTGCATGTGTCTTTATAGCAGCATGATTTA  
TAATCCTTTGGGTATATACCCAGTAATGGGATGGCTGGGTCAAATGGTAT  
TTCTAGTCTAGATCCTTGAGGAATTGCCACACTGTCTACCACAATGGTT  
GAATTAGTTTATAGCCCCACCAACAGTGTAAAAGCATTCTTATTTCTCCA  
CATCTCTCCAGCACCTGTTGTTTCGTGACTTTTTAGTGATTGCCATTCT  
AACTGGCACCACAGTAAATTTTATAGATTTTATAAGCAAATGTATTTA  
CTGTGCAAGAATTGGTTTATTTTTTAAACCATGTGTTGCAAACATACAAT  
GGTTAATTGTGATATTTGCTCAGTACAAGATCATCAGATCACTACACAGA  
CTTGAGGTAATTCACCTAAAAGCAAAGAGAACTGACCCACATTAAGTG  
AGAAGTCTTTACTTATTTATTCCTATAAACGAGCCAATATGAAGAGAAG  
GCCTTAATGTGGTTAACTATGTAATTTTTTCTGACTTTTGAAATACTG  
AGAAGAGCTCATGACTCTCCCATCTCCTAATTTCTACCTTGGTGGATTTTA  
GACTGACCACAACTCATGGGTAAATGAGGGAAGACGAATAAGAAACCTTG  
CTTTTTTTCTCCTTGTTTTTGGCTGGCTGCAGTGGCTCACACCTGTAA  
TCTCATCACTTTGGGAGGCCAAGGTGGGAAGATCACTTGAGCTCAGGATT  
TCAAAACTGGCTGGGCAACATAGTGAGACCCCATCTCAAAAAAAAAAA  
AAAAAAAAAAAAAGGCGACAGGCGGTGCGTGCCTGTAATCCTACCTACTC  
AAGAAGCCGAGGTGGAAAGATCACTTGAGCATGGGAGGTCAAAGCTGCAG  
TGAACCTTGATTGCACCACCTTATTCCAGCCTGGGTGACAAAGCAGGACG  
CTGCCCTCAAGAAAACAAAAACAAACCTTAATTTTTTGGCTATTCTTTTC  
TGGTAAGAAATGGTATAGAGATGGGGATGAGGATGGCTATTGTATGAGAGA  
GCAAAACAGGGTCCAAGCAGTGCTCTGGGCTGTCTAAGGACCAGTAGTCAG  
CTTAACCTCTCAAATTTCCAGGGAAGGAGTTCGGAGTGGTAGAATATCCT

FIG. 3 (19 of 52)

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GGGTATGCCCAAAGCATCACCTTGCAAATAGCCTGTGATGAATAATTTG  
 TTCATTTGTTATGACTGGAACTGGCTTTGTGTATGCCAGAGAATGGGGG  
 CAGGAAAGAGAGATTGGTGTCTTGAGCTCTCTGTGCCTCTGGGGCAGTGA  
 TGCTTTTCTCTCATGTGGAAGGAGAGCATGACTGAAAAGGTGCACAAAT  
 AAGGTGTCTGTGAGAGAAATTAACCTTCCAGATACAGAGACACAACCTTC  
 CCCAAGAGGTCTCATTTGCTCTGCCTTTTTTCTTTTTTTTCTTTCT  
 AQCATTAAACAGAACTGATTATGACCTCAAAGAGAGGAGAAAGCGA  
 CTCTCCCCACCCTAGAGCTAGTTAACCACCATATCTTCTAGATATCCTT  
 GAGAGCAATGTAACCC

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GTGAACCTCGTTTTACCTGTGTAGCAGACCAAGCCGACAGACAAAATCCNTC  
 AGACACCAAATTAAGAAGGAAGGGCTTTATTGGGCCTGGAGCTGCGGCA  
 AGACTCACGTCTCCAACAACCGAGCTCCCCGAGTGTGCAATTCCTGTCCC  
 TTTAAGGGCTCACAACTCTAAGGCGGTCCACATGAGAGAGTCGTGATAG  
 ATTGAGCAAGCAGGGGGTATGTGACTGGGGGCTGCATGCACCTGTAGTTA  
 GAATGGAAACAGAACATGACAGGGATCTTCACAGTGCTTTTCTATGCAAA  
 TAACCGATTAGATCAGGGGTGATCTTTACCAGGCCAGGGTGTGTACC  
 GGGCTGTCTGCTTGTGGATTTCAATTTCTGCCTTTTAGTTATTACTTCTTT  
 CTTTGGAGGCAGAAATTGGGCATAAGACAATATGAGGGGTGGTCTCCTCT  
 CTTACCTGCGGGGAGTGAGCTCAAACCTCTTAAAGGAGTTACCTGCCTTC  
 CATCATCAGGGAAGCAGGAAATCTTGCTTCTCTTGTGGAAGCAAGTAAA  
 ACTCAAAACAAACAAAGAAAAAACAGGGAGTTGTACAGCAAAATAAACT  
 TTTGATTTTACCAAATTTTGGGAGATCAGGAATCTCTGAAGGAGATGC  
 TTTACAGACTCAGCAAAATTTCTCTGTTGGTTTGAAGCATAAAGTTAGCTC  
 ATGCTGGTACCAAACACCACTAGGAGATTTGTCAAAGGTAAGAGGCATCT  
 CCACTCAGAATCCCTTCGTGGTTACCAACATGTGAACCTTGGAAATCTGA  
 GACAGGTCTCAGTTAATTTAGAAAGTTTATTTTGGCACGGTTGAGGACAC  
 CCACCATGACAGAGCATCAGGAGGTCTTGACCACATGTGCTCAGGGTGG  
 TCTGAGCACAGCTTGGTTTTACACATTTTAGGGAGACATGAGACATCAGT  
 GAATATATGTAAGATGTACACTGGTTCCCTCCAGAAAGGCAGAACAACTT  
 GAAGCAGGGAGGGAGCTTCCAGGTCACAGGTAGGTGAGAGACAAACAATT  
 GCATTTCTCTGAGTGTCTGATTAGCCTTTCAAAGGAGGCAATCAGATAT  
 GCATTTATCACAGTGAGCAGAGGGGTGACTTTGAATAGAATGGGAGGCAG  
 GTTTGCCCTAAGCAGTTCCCAGCTTGACTTTTCCCTTTAGCTTAGTGATT  
 TGGAGGCCCAAGATTTATTTTCTTCTACATCACTGTGGGCAGCTGACT  
 AGGAAAGCTTTGTAGGACTGGTGGGCAGTGTGAGAGCCAGTGGGGGGTG  
 GTGGTCTGTGCCAATGGTAGCAACCACCTGTGAGGCTGAGTAAACTCAT  
 TTCCCAACCTCCTCTAGCAGCCCCAGTGGAGATACAGAGGAAGCAGACTA  
 GCGATACAACCCAGCCTGAAGTTTTGTCTGGTGAGTGTAAATGGAATAAAA  
 ATGGGAAGGGTGTGAGAGACCCAGCAAGAAAATGGTTGAAGAGATGGGG  
 CACAGAAATTAAGCTGGATCAAAAAGGACGGAAAAGCAGAAAGGGCCGAT  
 AGAGAGAGGGGATATCTATGGGTTCCGCGATTCTGAAAAGGACAAATCACT  
 GGTGCTTTGAGAAGAGAGAGGGGTGAGAAAGCAGGAAGGCTGGAGGCTGTC  
 ATCCAAGAGGCGGACATCTGTGAACATGATTCCAAGAGTCACCAGACCAT  
 GGGGGTGGCCAAAGGGAGTGCCTCTTCTCACTCTCTACTCTTAATTCCTT  
 GTACTCAAGATAATAAGTTCCAGAAAGAGAAGTACCCATATTTAATTCAT  
 CTGTGCTCTTCTAGCAGTACTAAAAATATTAATATGAAAGGTATCAAACCT  
 TTGAGAATGTGTGCTGCTAAATTTGTTAAGGATGCTGGAAAACCTCAAGACG  
 TCCCTGATCCTGAGCCTGAGTATGAGCCTGTGGTGAGCCCAATGCAGGTC  
 TCCATTGAGACAAAGGCTCAGGGAACGGATGAGACCTAGGGACAGAGAT  
 GCATGCTGGAGCAGCATTCCCCATCCCTACTGCAGCTCAGGCCAGCTGAC  
 TGCTTTATGAGTAAACGTTACCAGGGAACACTTTGCAGTCTTAACACACA  
 TGCCACCTGTGACCACTGATCCCTGTTGGGTGACCACTGACATCAGAGA  
 TTCCGATGGCAGCAATGAAGACAAGGCTATCCTCATTAGGAAGGAAAGGAA  
 GGAGGAGGGAGGAGGGCAACGAATCTTTCTGCTTGTCAACCACGTCCA  
 TCTCTGTTAGTGATTTCCTATGTGTGACTTTGTTTATCTTTATAATAAC  
 TCTGAGAGGTAGTCTTGATGTCCACATTTTGAACATGAGGACATCCAGC  
 CAGGAAGTTGAGTTCTGGGGACATAGCTGAGAGGGCAAAGCTACATATAA  
 ACCCTCTTTGTTTTTCTGGCTTATCCACTGAGTGCCCCCTGCAATCCA  
 CCAGCCCCATTTGTGAAGTCATACTATAGGTAAGTTGGCACAGGAGGAGT

FIG. 3 (20 of 52)

GGATGTGGGGCGATTGTTGACAGCTCTCCAGGAACTTACACACTGGTGAG  
GAGGGCCAGGTATGTTCTGACCAGTCACAATCAAAGCAACCTCCTACTA  
ATCAGGGAGGCTTGGTACCTGGGGAATGCTATGTTGAAAGGTTCTTTCT  
GGGTTTTAAATGATGGGTCTATTTCTTATTCTTAAGATTGCTTTTTT  
CTGGCTAGAACTTAAAAGAAAATTTTCAGTAAAATTTCCCTTCCCTGGCAC  
AAAGTGAGCTTGAAATGAATTTCCAGGTGGCCTTGATACTTTAAAAATATT  
GCCTCTATAAAATCAACCTTTAGAAGAAGGAAGTCAAAGAACATGCTAG  
ATTTCAAAAAGGTTAAATTCCTTGAAATCCAGTTATCTACAGGACAATGTT  
GTCAAAGAAAAAATTTATTTGGCCAGGCACGGCGGCTCATGCCTATAATCC  
CAGCACTTTGGGAGGCTGAGGCAGGTGATCACCTGAGGTGAGGAGTTCGA  
GACCAGCCTGGCCAACATGGTGAAACCCCATCTCTACTAAAAATACAAAA  
AAAATTAGCCAGGTGTGGTGGTGGGCACCTGTAATCCAGCTACACGGGA  
GGCTGAGGCAGGAGAATCGCTTGAACCCGGGAGGAGGAAGTTCAGTGAG  
CCAAGTTCAAGCCACTGCACCCAGCCTGGGCAACAGAGCAAGACTTTGT  
CTCCAAAAAATAAATTTCAATGATATTTTTAAATTCATGGTAAGGAA  
GATTTCAATCAGAACCAGCACAGAAGATATAGGAAACACTGCAATGGGAC  
TTTGCGGTGGGGGAGAGAGATTGAACACAACACTACATATACAGCACGGGCA  
AGGACATATTCATAGCCAGGAAGCAGAGCAAAGATCAGTGGATGCGAAAT  
TACTAAGAGGAAACATGAAAAATAAGGGAGCTTCTGCCTAAACCCACCTA  
ACCGGATCCTTGCTGAAGACAGGACAGGGTGATTGGACACCCTTTGGGG  
ATGGTGGAGGATGGGGAATCCAGTGAGATTTCAAGGGTGATGCGATATTG  
AACATACAAAGTTCTTGCTAAAAAAGGATTTTACAAGAAAGTGACAAAT  
GTGCCTGGGACAAGGTGCAGGAGCCCGACGGAGATGTGGTCCAGCAGAGA  
ATATGTGCGGAGATGATAGGTGAGTTCTCTGACGAAGGATATATGCTGAT  
CCAGCCAGGGTGAAATGCTCAGAGAAAGCACGGAGGGGCTATGTCCGTTG  
CCCCAGTCTCCACGCGGTCAAATCTGATCCCGTTGTGAGTGTGGCCGTTT  
GTAGAAAGCAATCAGGGGGGGTCCCTCCCC

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AAATATATTTTTTATANNATNTGAGACAGGTTCTCACTAGGTTGCCCAG  
GCTGGTCTTGAATTCCTGCCTTCAAGTGACTCTCCACCTTAGCCCTACTG  
CATAGCTGGGATTACAGGCACAAACCACTGCATGCAGCTAATTTGCTTC  
TCATTCAGCACTTTTTATTCCTGATTATATGTATATGTATATCTGCA  
TCATCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTATATATATATATAT  
ATGGAAATATCTCTCTCTCTCTCTCTCTCTATATATATATATGAAATATATCT  
CAGTCTCTCCTATCCTCCTTTAATCAGTTTTGCTATCCTGTCAATTCCTC  
CAACGAGTGTGATGTTGTGAAATATATATTTGTTCTTCATCTCCTGTTTC  
CTGACATACAGCTTTTAAAAACCCCTTGAATCTCTGGAATAATAAGAGTG  
TCTTTTGCATGCTAATAGATGACTGCTGGCTGGCAGCCCCAATGCAGTAG  
CTTCATGATGGGGTTTGTACAGGAAAGACCAAGGCAGGATTGGAGACTT  
GAGACTGTTAGCCCCACTCCCCAACCACTGGAGGGAGTGGAGGGGCTGAA  
GGTTGTGTGAGTCACCAATGGCCAATGGTTCCGTCAATCATGTGTATGTA  
ATAAAGCCACTCTTAAAAACCCAAAAAGGACAGGGTTTGAAGGGCTCCC  
AGATAGCTGGACACATGAAGGTTCTTGGAGGGTGGTGGCCCCAGAGGGGCA  
TGGAAGCTCCACACCCCTTCTCATATGCTTTGCTCTGCGCATCTCTTCAT  
CTGGTGTTCATCTGTATCCTTTGTAATATCTTTAGAATAAACTGGTAAA  
CTTAAGTGTTTTCTGAGTTCTGTGAGCTGCTTAGCAAATTCACGGAAC  
CCGAGGGAAGCAAACCCAGATTTATAGCCATCAGTCAGAAGCATAGGTGA  
CAACCTACCACTTTGTAACCTGGCACCTGAAGTGGGAGGCAGTCTTGTGAGA  
CTGAGCCCTCAACCTGTGGGATCTAACGCTAATCCAGGTAGATAGTGTT  
GGAGTGAATTAGGACACCCAACTGGTGTGCGCTGCTGGAGGACTAGTGGT  
GGGAGAAATCCCCAAGCATTTCCGTGACTAGAGGTACAGAAGAACTCAG  
TGTTGAGGTGTTGTACAGTATGGTAGGGAATACTGCGTCTGGTTTTTTC  
CTTTTACAATCAGTTAAATATTTAACACAAGTCTACTGTATATTAGTAAA  
AGGGTTACATTTTTTAAATGTCTTGACAGTTGCACTTTGACAACTTCCATA  
TCAATCACTTTTTTTCGTGTCCGTTTGAACCAAATCACTTGGGATACC  
ATGAACCAGGCTGCAGCGTATTTCCCGAGGCTTGAAGCTTGGAGGCCAT  
TTTGCCAGCCNTAATCCCTGTGAATACCAGGCTTCTGGATTAAAAAAT  
AGACTTGAGGCCAGGCTGGTGGCTCACACCTGTAAGCCAGCACTTTGG  
GAGGCAGAGCGGATAGATCACAAGGTTAGGAGTTCAGAGACCAGCGTGGC  
CAACATGGTGAAACCCGCTCTCTACTAAATATACAAAAAATAATAGCCG

FIG. 3 (21 of 52)

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GGCGTGATGTTACAGCAGTAGTAGTGCCAGATACTCAGGAGGCTGAGGCG  
GAGAAATACCTTGAACCTGGGAGGCAGAGGTTGAAATGAGTCAAGATCGTG  
CCACTGCCTCCAGCTTGGGCGACAGAGTGAGACTCAGTTTTTCAGGGGAG  
TTAAAACAATACAAAAAAGAAAAAGACTTGAACAATGAGGCTCCACTGG  
ATGGATTTAGGGGAATTACAGGAAGCAGGACCTGACGGTGCAATGCCACA  
CTCCACCTGTCCAGAATTGGACCTCACCAGGGAGGTCTGTGGGGACAGG  
GAGAGGCCCTCTGCCTCCACCCCTCCTCTACTCCCCAACCCCTGAGTCA  
GGCTGAATGTAGTAAACCTGGAACAGAAAAGTTTCAAGTTTGGCAATAGSTA  
TCTGAAGGACTCCAGGTGCTTCTCCCTTGATTCAAAATTTTACTTATAAA  
AAAAATTATAAGAAAATTCTACTTAAAAGAAATAATCAGGGAGGTACAAC  
AAATTGTACTTTTTTTTTTTTTTTTTTTTTTTTGAATGGAGTCTCACTG  
TTGCCCATGCTGGAGTACAGTAGTGTGATCTCGGCTCACTGCAACCTCCG  
CCTCCTAGGTTCAAGTGATTTTCTACTTCAGCCTCCCAAGTAGCTGCGA  
TTACAGGTGTGTGCCACCACACCCGGCTAATTTTGTATTTTGGTAGAG  
ACGGGGTTTCAACATGTTAACCAAGATGGTCTCGAACTCTGACCTCAGG  
TGACCCACCTGCCTCAGACTCCCAAGTGTGGGATTACAGGGGTGAGCC  
ACTAAGCCCAGCCATTGTACATATTTTGTGGGTATTTACTAAAACATTAT  
TCAAAATAGTAAAAAAATTGAAATAAACTGGGGACTGGTTAAATAATT  
TTGGGTACAACCACATGATGGAATACTATACAGCCATTAAAAATTACATT  
GAGGCCAGGTGTGGTGGCTCATGCTTGTAACTTAGCACTTTGGGAGGCC  
AAAGTGGGAGGATTGCTTGGACCCAGGAGCTCAAGACCAGCTTGGGCAAT  
GTGGCAAAACCCCTGTCTCTAAAAAATAACAAAAAATTAAAAAGCT  
GGGTGTGGAGGCACACACTCTAGTCCAGCTACTCAAGGGCTAAGGTG  
GGAAGATCACTTGAACCGGGGAGGTCAAGGCTGCAGTGACCCAAAATCGG  
GTCAATTGCACTCCAGCCTGGGCAACAAAGCAAGACCTGTCTCAAAAAA  
AAAAAATACATTGAAGAATATCTTACGGTATGGATAAATATTCATTTTA  
CAGTGATAGATGCAAAATAAAGCAAATTACAAAATATACAGTTTAATTCC  
AACTTTGATACTACATATGTATATATGAATACATGCATATGTTATGTATG  
TATATGTAAATATAACAATATATGTTCTATATATGGATATTATATTTTA  
CACATACATACACATATATAATATCTTCTCTAGAGAGCAGAAAGAGAG  
TAGACAGATAAATGAAGATAGGATACAACTCCAGTCCAGCTCAACCTAGGG  
GACTTGTTTTAAAGCCTCAGGAGAGAGAAGTTGGGACTAGAAAGCAAGGC  
AGCTATTTGTAAGCATCTTTGTGTTTCATGCTATTGGGGTGGGAAACAAC  
AGCACAACCTTTTGAAGCCCCCTTTCTACTACCCCAACAACTGCAGAGCA  
GCTTTAGGACCCTCAGAGTTCAAGAAGACCATTTCAGAGTAGAAGAAGT  
AAAAACATGTATGAACCTGACCCTGAGCTCATGGACTGTGCCATGAGGGA  
AATTCCTAAAAACAGCAGGAGAGGCCCTGGAGGAAGGCAGAGGCCCTGCAT  
CAGCAAGTCCAGGCAAAAGCCTGCATTCCATAGATGCTCATCTCTCTGGC  
TGGTGAGGTCTAAAGACGTTTGGTCTCAATATTAAGTCTCGTGAGAGAGG  
TCACAAACCCAGTCCCTTGGCCACAAAAGGAAATAAATTCTGGCTTGAGA  
CATTAGGGAGGAACAGGGCAAGGGGAGGTTCAAGAAAGTTTTAATGGATG  
AGATGATATTTAAGCAAGGCCCTGGAAAATGAGAAATTTCAACCAATAGCC  
ATATGGTAGGTAGAGAAAGCAAAGATAAGGAGGGGGCAAGTGCAAGGGGCA  
ACATCAGATATGACCAGGGTGTCTGGGGCATGGCTGATGGAGAAGAAGA  
TTAGACTGGAGTTTGGGAATGCCACAGTATCGAGGTTGGATTTAATCCTA  
TGGGTAAATAAAGCCAACTGTTCAACCCCAACCCACTTGCAATATGGCTC  
CAAAATAGCAGGTGTTTGATAAAATGACTACTTTTACTCTACTATTCCCT  
CCCTCTTAAGAAGAAAAAGAAAGTGGAGGCTCAGAGAAAGGCAGTGGCTT  
GTCCCAATCACACTATGATTTGGCCACAAAACAGAACGAAATGTTACAC  
CCAAAAATGCTGCCTCCACCTCCCTTCTTGCTTCTCCTCCCTGCTGGACT  
ACAGACTATCTCAAGAGTGACGTACACCATCAGGGCTTCAGCTTTTCCCC  
GAAACAATGCCAAAATATTAGCCATACGTCACTGTAGTAAGAGCCCTGAA  
TTGGGAATCCCAGCTTTGACGCAGACATGCTGATTGACTCTGTGACCATT  
CTCTTCACCTTCTCCACTCTATTCTTCCCCACCTGTAAAGTGAGGTCCTTT  
CCAGTTATAAAAACAGATGATGCTATTGTCCTGTTTGTATCTAATCTTG  
CTGTGTTATAAAAAAATAAGGCTCTGTACATTCTCTTGGCCAATTC  
CCTTCTTATCTCTACTTCCACAGCCCTTTTCTACAGAAAACAGCAT  
TGTCTTCTGGATCCATCTCTTAAGAAAGCGCTTTGCCTCCCCGTTATT  
TAGGTGATAAGAAAGTGTCTTAGATGACAGCCCTGGAATGGGCTGGAGGCA  
ACAAAAAGCAAGTGAATAGACAGTTACAGCGACGACAATAATAACAAC



CAACACCTCTCACTAAAGAGAAAGAAATAAAAAAGAAAATTAAAAATCTGC  
CGCAATGCCACACAGTCATTGAATAACTGCATGTGTACAGCACTTGGTT  
ACTTTTACATACTTCATATTTTAGCCTTCATAGCAGCTCACAGGGGTGGA  
TTTAATTTTGTAGTCCAACCTCCTGTCACGGTGCCTGGCACAAGTATAATAA  
ATGTTCTGTGAATAAATGACCCTCTTTTATAGATGAGGAAATCGAGGCTCA  
AGGAGAACAAGCAATGTAATGTCCCCCTCCTGTTGAGCCATCTGCCTTTC  
ACGCCACTGAATGCAGTAGTCCCTCAGTGCCCTGAACCTTGACCTCTTCTG  
CTTTTCGGACTGGTCTCTTCTAATCCCGTTGTGACTCACTACACCACCTCT  
CCTGCATATGACATCTACATTTTAAAAACAAACCGTATGGAAATAACACAT  
TAGTCGGCTTGTTCCTCCACCCCGCAAAAAAAGGCCTCTTTATAACA  
GAAACTTCTCAGGCTGGTAGGGGAATTTATTCCCCCATTTATGGTAGAA  
AGGCCCTAACCTTGGACCTCACGCCATAGCTATTACATGGGGGAATGAT  
GAATAACATGGGGAGCAGCATGTAAATATCATTGAGCCGTAGTCCAGACC  
TATAACACATC

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GGGGGAGCTGCATGTGCCTGTGCGAGATCTGGGGGAGGAACAGGAAGATCA  
AGAGTTCTGTGTAGGACATGTTAAGTTGAAGGTGCTTACAGGATAGCCAG  
ATGAAGCATCAGGTGTGCAGTCAAAGATATGAGTCTGGAGCAGCACATCC  
TAAGTCACCTCCTGCACCAACACAGAACTTCCAGGCCACTCACTTGAGCT  
CTCCCAAATAGTTTCCAAGTGTCTATTATGTTAATAACCTATGAGCTTGAA  
CACCAGATTCAAACCCCACTGCATGGCTTTTAAAGACCATCTCAAGGGCT  
TGACACTCCAGGGAGCCAACTAAAGATGCCTGGTCTTACCATCAACCTCC  
ACCCCATTTTTATAGAAAATGTTTCTACCTGTCTTAAGGCAGGGTCTCTG  
CCCCACTCCAGGCCCTTTAGATCCCCAATATTCCTCTCTCCCTGAACCA  
AAACCTTCATCATCTTCCAGCATGGGTGGGGCTCCATTCTTGCTTCTGC  
TCCCCCTGAGCAGAAGCAAGTTTCTCCCAACTTGACCTGATTCTCTCTCTA  
AGTACCAGTCAGTCTTGTGTTCTGGAATGAGAGAAAAAGACAGAGTGAG  
AGAGACAATCCAGAACTCTTGCTCACTCACAGCTAGGCTGGGCATCTGGG  
AGGATGGCTGTGTCCATGGGAACCTGGGAAAAGCCACACCCTTGGCAGCC  
TGGTCACCCACCTGTCTCCTGGCAGATTCCGCACTGCTCTCTTGACCC  
TCTACCAGGGCTAACCGGCTGTCTCACTCTCCCCAGCATGTCTTCCCAG  
CCCCTCTCTAATTATTACATTTCCCTTACATAAACTGCCCTTCTCTCCC  
AATCACCACATGTTCACTTCCCACCCAGCTGTCAAAGTCTGGCTCAACCT  
CATTCTTGAAAAGGAAAAAACAACAAACAACAACAACAAGCAAAAA  
ACCTATGATGGATTAAGAACACACTTCATTCCAGGAACATGCTTATCTCC  
TCTAACTCTCACAACAACCTACAGCAGGTAGGTGTTATCACACCCATCTCT  
CAGGTGAGAAAACAGGCTCAACGAGTGCAGGAGGACACAGCAAGTCAGTG  
ACAAAGCTTAAATTCAAGCCCAAGCCTGTTGGCAACCAACGTCTGTACCC  
TTGATAGCTACCTCATTACCAACCAATCCAGTGGCCTCAGGCTGGCTG  
CACACTGGGATCACCTGGTGGCCAGACCACATCTTAGACCAGTCATACAG  
AATCTCTTGGGCTGGGATCCTCCACGGTACATTTAAGGGTCCCAGGTG  
AGTTCCACCATGGACCCAGAATTGAGGACCAATACCGTATACCATCTCC  
TTCTTCATCTCTTCTAAGGCATCTCTTACTCGCTGTGCACTCCCATACCA  
CTTTGTTCAATCATCCAATCATTCACTTATTGAGTCAGTTAGTCAGGAGC  
TACTCACTAGTCCCCTGCCAGGTCTAGTCATGACATAGGGCTCTGGGGA  
CCAACAAGAAGCAGGACCCATGCCTCCTGCTCTCATGGAGCTTGCTCTGC  
AGCAGAGGAAGCAGTCAGTGAGATGTAGCAAATGTGAAATGTGCACAGAT  
GGGAAAAGCAAACTTTAAAACCTTTTAGGACAAAATACACAAGAAATCTT  
TGCAACTTTGGGACAGGAAGGAACAACATTCCTTACACATGACACCAAG  
GAATCAACCATAAATAAAAAGGTGATCAATTTGACCTCATTTAAGTGTTA  
AGCTTTTTCATTGAGAGACACCATTAAAAATTAAAAATACATGCCACAA  
ACTGGGATACAAATATTTACAACACTTATGTCTCACAAGGATTAGTTTTT  
AGAATATATAAAGAACTCCCGGCCGGGTATGGCCGCGCACGCTGGAATCT  
CAGCACTTTGGGAGGCCAGCGGATCATAGGTCAGGAGTTCAAGACCA  
GCCTGGCCAACATGGCAAACTCCGTCTCTACTAAAAATACAAAAATTAG  
CCAGGCATGGTGGCGGGCGCCTGTAATCCCAGCTACTCAGGAACTGAGG  
CAGGAGAATCACTTGAGCCCAGAAAACAGAAGTTGCAGTGAGCTGAGCTC  
ACATCACTGTAAGCCTCGGTGACAGAGTAAGACTGTCAAAAAACGAAAA  
CAAAAAACAAAACCTCTACAAATAAATAAGAAAAAATAGCCAGCAGGA  
AAAAGTATATACATTTTCAAAAAGAATAAATACATTCTGTCAGTTTTCTA

FIG. 3 (23 of 52)

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ACATATATTTTTTAAGAGTAAATACAAATGGTTAGGAAACATTTTTTAAA  
ATGCCCAACCTCATTAAAAATTATAGAAGTGAAAATTAAGCCACAATAAG  
ATACGATTTTATACCAAATACAGTGTCAACACTTTGCAAGTCTGACCTCA  
CCAAGTGTACCAGACGTGTGCACTGACGTGGCTGCTGAGATACTGATGG  
TGGGTCTTAAATCTGTACTACAAACAATTGCAATAAAATGTAATAAATA  
TACAAATAGGTGGAGCAGGAAGTGACCTGCAACCATATAGCAGATAGGGCA  
GGAAAAAGCCTATGAAAAGCTGACATCAAAGGGATAAGTTCAGTTACCCA  
GCTGAAGGGAAGGAGGGTGTTCAGATAGAGGAAGGATAAGCATGACCTA  
TTCAAGGCCAGTGAAAGAAGCGTGCAACGGCCAAGTCAGGAGAACCCTGAA  
ATTGTGTCAAAGAGCTTGGATGCAAAGAGCCGTGGGAGACTATTGGGGGT  
TTAAGCAGGGATATAATATTCAATTCAAGCATGCAGTAAAAGGTCACTGG  
CACCTGCCATGGGCCAGGACTCGGGCTCTACATGATTGCGTCTGTTTTGG  
AAATATCACCTGGCTGTGAGATGAAGAACAGGTAGGAGGGTCACAAAAC  
TTGAAGCAGAGAGACTGTTGAGGAAGTAAGCTGTTTTGTGTGGACTGTG  
GCAATCACAGAGGCAGAGGATATAAATGCACAGAGACACAAGGCATGTGG  
GAGGCAGAAGGAATCAAATACAATGAGTGATCAGATGTGGGGTAGAGTG  
GTGAGTGAGAGACATACTCAAGGTGACACGCCAGGTATCTGGGTGGAT  
GGTAAGACATTCACTGGACTAGGATCGAGGAANGAGGTGGGGAATGGGACC  
ATACCTGCAGTTTATAAGGGGTGGACGAGGGAAGATTATCGGGGAGACTG  
AGAGAGGAATAGACAAAGGAATCCCGGTGCAGTATTACAGAACTGGGGT  
GGGAGGGGGTGTANTTCAAAAAGGAAAGAAAATTGTCAAATAGTATGAA  
ATGCTGCAGAGAAAACACCGGATTTTTTTTTTAAGCTTAGAATTATTCAT  
TGACTATGTGAATAAGAATAACTTTTATGAAAGAAGTTTGTCTAAGTAG  
TAGGAAGAAGCAAAATTGTTGAGGGCTGATGAGTGGGAGGAGAAGTAATT  
GAAGGCACTCTTTCAAGAGAAACAAAGCAGAAGGTGAGGAGAATACTAAT  
GAAGGAGTTACGGCCTTCACTATTTTGTCTTTAGATAAGCAAGACT  
TGAGTGGGTCTGGTGAGGAGAAACAAGTAGAGTACAAAGTTAAAGGAGAG  
ACAGACAGAGATAGAGATAGGGACAGAGAGAGAGACAGAGACAGAGCACA  
AAAGAGCAAGGTCCCTGAGAAACACGGCCTTCTGTTTAAACCCAGCCAG  
ATGTATTGCAATTCAATTCAGTACTAACCACCCAGAGTTTGTGTAGACT  
CTACAAGTTAAAGAGCATGGTCCCAACAAGACTGCTTCTACGTGAGATG  
CCAGGCACACTTCAGGGGTCCCAAGCCACTCATGTTTTTTGAATGACTG  
CCATAAGTTCAAAAATTCCCACAATTCTCTCAGATTCAATAACTGGGTAT  
AACCCTCATAGAAGTCAAGAAAATGCTATCATTATTATTACAATTTTAT  
TATAAAGGATACAAATCAGAAGGACTAGCCAAATGAGGAGACACATAGAG  
AGAGGACTAGTAAAAAACAGAGCTTCTGCGTCTACCTTCAAGGAATCAG  
GATGCACACCCCTCCAGCACATCAAGTGCTCATCAACCAGGAAGTTCT  
CTGAGCTCCAATGTCCAGAGATTTAGGGAGGATTCATTACATAGGTATC  
ATTGATTAAATCATTGGCCATGTACTTGAAGTCAATCTCCAGTGTCCCTC  
TTCTCCCTAGAGGTCTGAAGGGTTGGCTAATATCATGTGGCTCAAAGCCC  
CAACTCTAATTACCTTTTTTGGTCTTTTCAGGGACTAGACCCCATCTGAA  
GCTATCTACAGGCCCTGCCATGAGTTAGCTCATTAACATAACAAAGACAC  
TTATATTACTCAGAAAATTCCAACAGTTTATAAGCTCCATGTGAGGAAC  
CTGGGACATAGATCAAATTCTTTTTTTTTTTTTTTTTTGGAGACAGGGT  
CTTGCTGTGTGCCCAGGCTAGAGTGCAAGGACAGATCACAGCTCAATGC  
AGCTTCAACTTCCAGGCTTAAGTGACCTTTCCACCTTAACCTTCCAAGT  
ATCTGGGACCACAGAAAATGGCTAATTATCCTGGCTGATTTTTAAACTTT  
TTTTTTTTGTAGGGATGGGATCGCCCTGTGTGGCAAGGTTGGTCTCAA  
CTCCTGGGTTCAAGCAATCATTCTGCCCTGGCCTCTGTGATGGTTAATAC  
TGAGTGTCAACTTGATTGGATTGAAGGATACAAAGTATTATTTTTGGGTG  
TGTCTGTGAGGGTGTGGCAAAGGAGATTACATTTGAGTCAGTGGACTGG  
GAAAGTCCACCCTTTCCAGTGGACTGGGAGACCCACCCTCAATCCAGGT  
AAACACAATCTAATCAGCTGCCAGTGTGGTCAGAATAAAGGAGGCAGAA  
GAACAGGGAAACACTAGACTGGCTTAGTCTTCCAGCCTACATCTTTCTCT  
CATGCTGAATGCTTCTACCTCGAACATCAGCCTCCAAGTTCTTCAGTT  
TTTGGACTCTTGGACCTTCAACCACAGATTGAAGACTGCAGTGTGGCTT  
CCCTGTTTTTGGGTTTTGGGACTCAGACTGGCTTCTTGCTCCTCAGCT  
TGCAGATGGCCAATTGTGGGACTTTAACTTGTGATCATGTGAGTCAATAT  
TCCTTAATAAACTCAGATATATATATATGTATCAGACATATATATATC  
CTATTGTATATTATACAGATATATAATATCCTATTATATACAGATATA

FIG. 3 (24 of 52)

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TAATATCCTATTATATATACAGGTATATATATATATATGTATCATATATA  
TATCCTATTGGTTCTATCCCTCTTGAGAATCCTGACTAATACAGCCTCCC  
AAAATGCTGAGATTACAGGAGTGAGCCACAGCCACCATGCCAGCCCCAA  
ATTCTTAATTATACAACAATGGGTCCAGAGATCAGGGCCTGGGTAGGATG  
CAGCAATAAGAAAACAGATGGTGGATGGGGACACATGTTGGAAGTGTCG  
AGGACATGGCTGAGGGAACCTCATAGGATGGTGTCTATTTTCATGGCTGAG  
TGTGAGGAACAGCATAAGGTCAAAATTTAGGTCAATGGTGAGTTTTTTA  
AATTGTTGCTGTGAACCCCAAAATCTGACCAGGTCTCAGTTAATTTAG  
AAAGTCTATTTTCCAAGGTTGAGAACACCCACCCACTCAGACAAGAGC  
ATCAGGAGGTCCTGACCACATGTGCCCAAGGTGGTAAGAGCACAGCTTGG  
TTTTATATATTTTAGGGAGACGTAAGTCATCAATCAATATATGTAAGATG  
TACACTGGTTCTGCCTAGAAAGGCAGGACAACTTGAAGCAGGGAGGGGGC  
TTCCATGTACAGGTAGGTGAGAGACAAACAGTTGCATTCTTTGAGTTTC  
TGATTATCCTTTCCAAAGGAGGCAATCAGATGTGCAATTATCTCAGTGAG  
CAGAGGGATGACTTTGAATAGAAAGACAGGCAGGTTTGCCTAAGAAGTT  
CCCAGCTTGCATTTTCTTTAGCTTTGTGATTGGAGGCGCCAAGATT  
ATTTTCTTTTACATTTCCCCCTTTCTTTTAAAGAACTTTTAAAGAA  
AGCTTTTAAAGAAATGAGTCTCTGGTCCCAGGTTTCATCTGAATTCT  
CGAGGGGAGGATGGTTTATCCTAAACGGGTGGTTCTGAATTTGAGAAAG  
TGCATTGTAC  
>Contig32  
AAAAGCCATACGAATGAGGAAGAATTAAGGGCCAGAACAAAACAAGAAGA  
TGAGGGAAAGTTTGAACCTTAGAGACTGGCTAAATGGTTGTGACCAA  
AATGCTGATAGTATACGGACAATGAAGTCCAGGGTGACAAAGTCTCAGA  
TGGAAATGGGGAATTTGTTGGGAACTGGGCAAAGGTCACCTTGCTATGA  
CTCAGCAAAGAAATTTGGGTGCATTGTGTTTCATGTCCTGGGGATCTGTGGA  
AGTTTGAATGTAAGAGTGATGACTTACGGTAGGGTATCTAGTGGAAGAAA  
CCTCTAAGCAACAAAGTGTGTTGCTTAGAAATTTCTTTCTTTCTTTTTT  
TTTTTTTTTGAGCTGGAGTTTTGCTGTGTGCGCCAGGCTGGAGCGCAGTG  
GCGCAATCTTGGCTCACTTCAAGCTCTGTCTCCTGGGTTTCATGCCATTCT  
CCTGCCTCAGCCTCCCAAGTAGCTGGGACTACAGGCGCCTGCCACCATAC  
CTGGCTAATTTTTTAGTATTTTAGTAGAGACGAGGTTTACCATGTTAGC  
CAAGATGGTCTCAATCTTCTGACCTCGTGATCCACCCGCCTTGGCCTCCC  
AAAATGCTGGGGTTACAAGCATGAGCCACCCGCCTGGCCTGCTTAGAAA  
TTTCTAAGCCAGGATATGGCCTGTCTGCTTCTAACAGCCTGTGCTCAGGG  
GTAAAGAAATGACTTAAAGTTGGAACCTATGTTTAAATGGAAGTAGAGT  
CTAAAAATTTGAAAATTTGCAGCCTGGCCTTGTGGCAGAGAAAGAATCC  
AAGTAGGCTGCAGAGCAATCATTGCTAGAGAGATTAGCATGACTAAAAGG  
GAGCCAGTGCTAATATTCAAGACAATGTTAAAAAGGCCTTGAGGGCATT  
TCAGAGATCTATGAAGCAGCCCCCTCCCATCAGGTGCAGAGGTTTGGTG  
CACTAGGCCCAGAGGTTTTATGGGCCANNGCCAGGGCCACACTGCTATGC  
ACAGCTTTGGGACACTGCTGCCCCGATCCAGGCCACTCTGCTCTGGCTCC  
ACCTTGGCTCAAACGGGCCAAGATAGAGCTTGGACCACTGCTCCCGAGG  
GCACAAGCCATAAGCCTTGGTGGTTTCCATGTGGTGTAAAGCCTGCAGGT  
GCCCAGAATGCAAGATTGAGGGAGCTTGGGCACTTCCACCTAAATTTAG  
AGGATGTGTGAGAAACCTAGGTTCCAGGCAGAAAGCATGATACAGGGGC  
AGAGCCCTTGACAGAGAACCTCTACTAGGGCAATGCCAAAGGAAAATGTGG  
GGTTGGAGTCTCACACATGGTCCCCACTGGGGCACTACCTGGTGATACT  
GTGGGAATGGGGCTGCTGCCCTCCAGACCCCAAGATGGTAGATGCACTGG  
CAGCTGGCACCTGAGCCTGGAAAAGCTGCAGGCACTCACTCCAACCCA  
TGAGATCAGCCACATGGGCTACTCCAGGGAAGCCACAGAGGCAGGGCT  
GTCTAAGCCCTTGGGAGCCTACCCCTTGAACCAGCTTGCAGGACATGGAA  
TCAAAGATTATGTTGCAGCTTAAAGGCTTAATGTTTTCCCTGTCAATTC  
AGGCTTGTGTGGGACCTGTTGCTTTTTTTTTTTTTTTTTTTTTTTTGGT  
CACAGGTGTTTTGAACCAGAACAAATTCATCTTGAATAGGGGCTGGGTAAA  
ATAAGGCTGAGACCTACTGAGCTGCATTCTAGGAGGTTAGGAATTCATA  
GTCACAGGAGGAGATAGGAGGTGGGCACAAGATACAGGTAGCGAAGACCT  
CGCTGATAAAATAAGTTGCAGTAAAGAAGCCAGCCAAAACCTCACAAAGCC  
AAAATGGTGATATGGTTTGGCTCTATGTCCCCACCCAAATCTCATCTCAA  
ATTATAATTCCATAATCCCCACATGTTGAGGGGAGGACCTGGTTGGAGG

FIG. 3 (25 of 52)

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TGATTGGATTATGGAGGCAATTTCCCCCATGCTGTTCTGGTGATACTGAG  
TGAGTTCTCATAAGATCTAATGGTTTTATAAGTGTGGAAAGTTCTCTCT  
ACACACATGCTCAGACTCTCTCTGAGCTTTATGAAGAAGGTACTTGCT  
TTCCTTTCTGCCATGATTGTAAGTTTCTGAGGCTTCCAGCTATGCAGA  
ACTGTGAGTCAATTAACCCGTTTTCTTTATACATTACCAGTCTTGGGCA  
JTTCTTTACAGCAGTGTGAGAACTGCTGGCGATGAGAGTGACCTCTGGTT  
GTCCTCACTGCTCATTATATGCTAATTATAATGTATTAGCATGCCAAAAG  
ACACTCCCACCATGACCCCAACAGTCATGCCTGTGCCGGTCTCAGCACC  
TGACAGTTTACAGATGGCATAGCAACGTCTAAAAGGTACCCCATATGGAC  
TAACAAGGGGAGGAACCCCTCAGCTCTGGGAAGTGCTTACCTCGTTCCAG  
AAAGCTTGTGAATAATCCACTGCTTGTTTAACATATAATTAAGAAATAAC  
TATTAAGCATCTTAGTTTACAGCAGCCCAAGCTGCTGTTCTGCCTATGGAG  
TAGCCATTCTTTATTCGTTACTTTCTTAATAAAATTGCTTTTACTTTAC  
TGTATGTAAGTCTGGAATTTCTTGTACGAGGTCCAGAGCCCTCTC  
TTGGGTCTGGATCGGGACCCCTTTCTGGTAACATTTTGACCAATTTCTCC  
CTTCTGGAATGGGAATGTTTACACAATGACTGTATCACTTTTGAATCTTG  
GAAGTAAATAATTTGTTTTGACTTTACAGCCTCATAGGTGGAAGGAACT  
TGACTTGAATTTAGATGAGACTTTGGACTTTGGGACTTTTGGGTGGGG  
CTGGAATGAGTTAAAGTTGGGGGGATTATTGGGAAGGCACGATTTTATT  
TTGCAATATGAGAAGCACATGAGATTGGGGGACCAAGGTGGAATAATA  
TGTTTGGATGTTTGCCCCCTCAAATCTCACATTGAAATGTAATCCCCA  
GTGTTGAAGTGAGGCTGCTGGAAAATGTTTGGATTACAAGGCTGTGAG  
CACATTGGATAAGACGTGTAGGNCCC

>Cont:1g33

CGCAGCTCGCTGGTTAATTTCTGTGGCTCCTGTGACCACTATTATAGCACC  
AGGTCTATGACCAGGAGAATTAGACTGGCATTAAATCAGAATAAGAGATT  
TTGCACCTGTAATAGACCTTATGACACCTAACCAACCCCATTTATTTACAA  
TTAAACAGGAACAGAGGGAATACTTTATCCAACCTCACACAAGCTGCTTTC  
CTCCCAGATCCATGCTTTTTTTCGTTTTATTATTTTTTAGAGATGGGGGCT  
TCACTATGTTGCCACACTGGACTAAACTCTGGGCCTCAAGTGATTGTC  
CTGCCTCAGCCTCCTGAATAGCTGGGACTACAGGGGCATGCCATCACACC  
TAGTTCATTTCTCTATTTAAATATACATGGCTTAAACTCCAACCTGGGA  
ACCCAAAACATTCAATTTGCTAAGAGTCTGGTGTCTACCACCTGAACTAG  
GCTGGCCACAGGAATTATAAAAGCTGAGAAATTCTTTAATAATAGTAACC  
AGGCAACACCATTGAAGGCTCATATGTAATAATCCATGCCTTCTCTTCTC  
CCAATCTCCATTCCCAAACCTTAGCCACTGGCTTCTGGCTGAGGCCTTACG  
CATACCTTCCGGGCTTGACACACCTTCTTCTACAGAAGACACACCTTG  
GGCATATCTACAGAAAGACCAGGCTTCTCTCTGGTCTTGGTAGAGGGCT  
ACTTTACTGTAACAGGGCCAGGGTGGAGAATTCTCTCTGAAGCTCCATC  
CCCTCTATAGGAAATGTGTTGACAATATTGAGAAGTAGGAGGATCAAG  
ACTTCTTGTGCTCAAATACCACTGTTCTCTTCTTACCCTGCCCTAACCC  
AGGAGCTTGTCAACCCCAAACCTCTGAGGTGATTTATGCCTTAATCAAGCAA  
ACTTCCCTCTTCAGAAAAGATGGCTCATTTTCCCTCAAAGTTGCCAGGA  
GCTGCCAAGTATTCTGCCAATTCACCTGGAGCACAATCAACAAATTCAG  
CCAGAACACAACCTACAGCTACTATTAGAACTATTATTATTAATAAATTCC  
TCTCCAAATCTAGCCCTTGACTTCGGATTTACGATTTCTCCCTTCCCTC  
CTAGAAACTTGATAAGTTTCCCGCGCTTCCCTTTTTCTAAGACTACATGT  
TTGTCACTTTATAAAGCAAAGGGGTGAATAAATGAACCAAATCAATAACT  
TCTGGAATATCTGCAACAAATAATATCAGCTATGCCATCTTTCACTA  
TTTTAGCAGTATCGAGTTGAATGAACATAGAAAAATACAAAACCTGAATT  
CTTCCCTGTAAATTTCCCGTTTTGACGACGCACTTGTAGCCACGTAGCCA  
CGCCTACTTAAGACAATTACAAAAGGCGAAGACTGACTCAGGCTTAA  
GCTGCCAGCCAGAGAGGGAGTCATTTCAATGGCGTTTGAGTCAGCAAAGG  
TATTGTCTCTCATCTCTGGCTATTAAAGTATTTTCTGTTGTTGTTTTTC  
TCTTTGGCTGTTTTCTCTCATATGCCCTTCTCTAAAGCTACAGCCTCTCC  
TTTCTTTTCTGTTCCCTCCCTGGTTTGGTATGTGACCTAGAATTACAGTC  
AGATTTGAGAAATGATTCTCTCATTTTGTGCTGATAAGGACTGATTCGTTT  
TACTGAGGGACGGCAGAACTAGTTTCTATGAGGGCATGGGTGAATACAA  
CTGAGGCTTCTCATGGGAGGGAATCTCTACTATCCAAAATATTAGGAGA  
AAATTGAAAATTTCCAACCTCTGTCTCTCTTACCTCTGTGTAAGGCAAA

FIG. 3 (26 of 52)

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TACCTTATCTTGTGGTGTTTTGTAACTCTTCAAACCTTTCATTGATTG  
AATGCCTGTTCTGGCAATACATTAGGTTGGGCACATAAGGAATACCAACA  
TAAATAAAACATTCTAAAAGAAGTTTACGATCTAATAAAGGAGACAGGTA  
CATAGCAAACCTAATTCAAAGGAGCTAGAAGATGGAGAAAATGCTGAATGT  
GGACTAAGTCATTCAACAAAGTTTTTCAGGAAGCACAAGAGGAGGGGCTC  
CCCTCACAGATATCTGGATTAGAGGCTGGCTGAGCTGATGGTGGCTGGTG  
TCTCTCTTTGCAAAAGTCAAGATGGCCAAAGTTCCAGACATGTTTGAAGA  
CCTGAAGAACTGTTACAGGTAAGGAATAAGATTTATCTCTTGTGATTTAA  
TGAGGGTTTTCAAGGCTCACCAAAATCCAGCTAGGCATAACAGTGGCCAGC  
ATGGGGGGCAGGCCGGCAGAGGTTGTAAAGATGTGTACTAGTCCTGAAGTC  
AGAGCAGGTTTCAGAGAAGACCCAGAAAACTAAGCATTTCAGCATGTTAAA  
CTGAGATTACATTGGCAGGGAGACCGCCATTTAGAAAAATTATTTTTGA  
GGTCTGCTGAGCCCTACATGAATATCAGCATCAACTTAGACACAGCCTCT  
GTTGAGATCACATGCCCTGATATAAGAATGGGTTTTACTGGTCCATTCTC  
AGGAAAACTTGATCTCATTAGGAACAGGAAATGGCTCCACAGCAAGCTG  
GGCATGTGAACCTACATATGCAGGCAAATCTCACTCAGATGTFAGAAGAAA  
GGTAAATGAACACAAAGATAAAATTACGGAACATATTAACTAACATGAT  
GTTTCCATTATCTGTAGTAAATACTAACACAACTAGGCTGTCAAAATTT  
TGCCTGGATATTTTACTAAGTATAAAATTATGAAATCTGTTTTAGTGAATA  
CATGAAAGTAATGTGTAACATATAATCTATTTGGTTAAATAAAAAGGAA  
GTGCTTCAAACCTTTCTTTTCTCTAAAGGAGCTTAACATTCTTCCCTGA  
ACTTCAATTAAGCTCTTCAATTTGTTAGCCAAGTCCAATTTTTACAGAT  
AAAGCACAGGTAAAGCTCAAAGCCTGTCTTGATGACTACTAATTCAGAT  
TAGTAAGATATGAATTACTCTACCTATGTGTATGTGTAGAAGTCCCTAAA  
TTTCAAAGATGACAGTAATGGCCATGTGTATGTGTGTGACCCACAACAT  
CATGGTCATTAAAGTACATTGGCCAGAGACCACACTGAAATAACAACAT  
TACATTTCTCATCATCTTATTTTGTACAGTGAAAAATGAAGAAGACAGTTCT  
CCATTGATCATCTGTCTCTGAATCAGGTAAGCAAATGACTGTAATTTCTCA  
TGGGACTGCTATTCTTACACAGTGGTTTCTTCATCCAAAGAGAACAGCAA  
TGACTTGAATCTTAAATACTTTTGTTTTACCCCTCACTAGAGGTCCAGAGA  
CCTGTCTTTTATTATAAGTGAGACCAGCTGCCTCTCTAAACTAATAGTTG  
ATGTGCAATTGGCTTCTCCAGAACAGAGCAGAACTATCCCAAATCCCTGA  
GAACTGGAGTCTCTTGGGGCAGGCTTCATCAGGATGTTAGTTATGCCATC  
CTGAGAAAAGGCCCGCAGGCCGCTTCACCAGGTGTCTGTCTCCTAATGTG  
ATGTGTTGTGGTTGTCTTCTCTGACACCAGCATCAGAGGTTAGAGAAAGT  
CTCCAAACATGAAGCTGAGAGAGAGGAAGCAAGCCAGTTGAAAGTGAGAA  
GTCTACAGCCACTCATCAATCTGTGTTATTGTGTTTGGAGACCACAAATA  
SACACTATAAGTACTGCCTAGTATGTCTTCAGTACTGGCTTTAAAGCTG  
TCCCCAAAGGAGTATTTCTAAATATTTTGTAGCATTGTTAAGCAGATTTT  
TAACCTCTGAGAGGGAACATAATTGAAAGCTACCACTCACTACAATCAT  
TGTTAACCTATTTAGTTACAACATCTCATTTTTGTAGCATGCAATAAATG  
AAAAATCTTCTTAAAAAATCATCTTTTATCTTGAAGGAGGAAGGAAG  
GTGAGACAAAAGGGAGAGAGGGAGGGAGCCATGAAACACCAGTTACC  
TAAGACCAGAATGGAGATCTTCTCACTACCTCTGTTGAATACAGCACCT  
ACTGAAAGAACTTTTCAATCCCTGACCATGAACAGCCTCTCAGCTTCTGTT  
TTCCTTCTCACAGAAATCCTTCTATCATGTAAGNTATGGCCCACTCCAT  
GAAGGCTGCATGGATCAATCTGTGTCTCTGAGTATCTCTGAAACCTCTAA  
AACATCCAAGCTTACCTTCAAGGAGAGCATGGTGGTAGTAGCAACCAACG  
GGAAGGTTCTGAAGAAGAGACGGTTGAGTTTAAAGCCAATCCATCACTGAT  
GATGACCTGGAGGCCATCGCCAATGACTCAGAGGAAGGTAAGGGGTCAAG  
CACAATAATATCTTTCTTTTACAGTTTAAAGCAAGTAGGGACAGTAGAAT  
TTAGGGGAAAAATTAACGTTGGAGTCAGAATAACAAGAAGACAACCAAGCA  
TTAGTCTGGTAACTATACAGAGGAAAAATTAATTTTATCCTTCTCCAGGA  
GGGAGAAATGAGCAGTGGCCTGAATCGAGAATACTTGCTCACAGCCATTA  
TTTCTTAGCCATATTGTAAAGGTCGTGTGACTTTTAGCCTTTCAGGAGAA  
AGCAGTAATAAGACCCTTACGAGCTATGTTCTCTCATACTAATATGC  
CTCCTTGGTCATGTTACATAATCTTTTGTGATTGATTCTCTACTGT  
AAAATGGAGATAATCAGAATCCCCCACTCATTGGATTGTTGTAAAGATTA  
AGAGTCTCAGGCTTTACAGACTGAGCTAGCTGGGCCCTCCTGACTGTTAT  
AAAGATTAAATGAGTCAACATCCCCCTAATCTTCTGACTAGAATAATGTCT

FIG. 3 (27 of 52)

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GGTACAAAGTAAGCACC\_AATAAATGTTAGCTATTACTATCATTATTAL  
 ATTATTTTATTTTTTTTTTTGAGATGGAGTCTCACTCTGTTGCCAGGC  
 TGGAGTGCAGTGGCGCAATCTTGGCTCACTGCAAGCTCTGCCTCCTGGGT  
 TCAGGCCATTTTCCTGCCTCAGCCTCCCGAGTAGCTGGGACAACAGGCAT  
 GTGCCACCATGCCAGCTAATTTTTTTGTATTTTATAGATAGATGGGGTT  
 TCACTGTGTAGCCAGGATGGTCTCTATTTCTGATCTCATGATCCGCCT  
 GCCTTGGCCTCCCAAAGTGCTGGGATTACAGGCGTGAGCCACCGCGCCCG  
 GCTATTATTATTATTACTACTACTACTACTATATGAATACTACCA  
 GCAATACTAATTTATTAATGACTGGATTATGTCTAAACCTCACAAGAATC  
 CTACCTTCTCATTTTACATAAAAGGAACTAAGCTCATTGAGATAGGTAA  
 ACTGCCCAATGGCATAACATCTGTAAGTGGGAGAGCCTCAAATCTAATTCA  
 GTTCTACCTGAGTAAAAAATCATGGTTTCTCCTCCATCCCTTTACTGTA  
 CAAGCCTCCACATGAACATAAAACCAATATTCTGTTTTTAAGATAATA  
 CCTAAGCAATAACGCATGTTACCTAGAAGGTTTTAAATGTAACACAAT  
 ATAAGAAAATAAAAATCACTCATATCGTCAGTGAGAGTTTACTACTGCCA  
 GCACTATGGTATGTTTCTTAAATCTTTGCTATACACATACCTACATGT  
 GAACAAATATGTCTAACATCAAGACCACACTATTTACAACCTTTATATCCA  
 GCTTTTCTGACTTAGCAATGTATTGATGACATTATGCATGCTTAGACCTC  
 C

>Contig34

GTATTCTATTCTCGGTTATAACACAATCACAGTGATTTGTCATATCTTTC  
 CAGGATTTGTTAATTTCACTTCTTCAGCTGTTTCCCCCTTGTTGGCTGGA  
 ACTGATTTTCTATCTTCTGGGAGAATCTTCAGCAAGCCAACCTCAGGATTT  
 GTTGGGTGCATTTTGTCAAGTCTAGGACCCAGGCTCTGGGTGACTGATTT  
 CCTCTAATTACCGAGCAATGTAAATGAGGAAGTCTGATTGTGTAAAGGT  
 GTTAAACTTTTGTGTGACGGCAAACTTTAATACCATGAATAGAGATTCC  
 AGAATTTTCCAACCTCTAACGGGATTCTTTCACTCCCTGACATTAGAAT  
 GTTAGAAAATCTACCACAAAACATCTGTGAGGCTATCTTACAAGGCCCGT  
 TTTTCAAAATAGTTTTTACAAGGATTGCTATTTGGGATGATAGTTTCAG  
 AAAGGCGCTATCAAAGTTAATTGATGATGTGTGCAAGCTGAAAGTTATAT  
 GTTAGAACTAGCAGTGATTTCAAAAATATCCCTTTTAGGCTTTTGTCTAA  
 TATATCTGCTCATTTTCAAAGTTCCCAATATTATAAACTTTTAAAGCA  
 GAAAGAAGAACCCTCCATTTCTGCTGGCCCCCTTCCCTGTTCAACTAAAA  
 GTATTTTCCCAGGCAATGCTATCCCAGGACTCACACTCCATCCATCCATC  
 ACCTACCATAAGTTCTTTGAAGGGCTCATTCTGAGCGCTTCCCTGAGTGCC  
 TGGGATCTGTTATTTCTCTCCATTTCTGCTGCTGCATGGTAGTCCAAGTC  
 CTCCTCCCTTTTCCCTAGGCCATTTGAATCATCTGCTAATTGTTTTC  
 TGATTGCCACGGAACTTCCCTCCATCCCTTCCCTCACATATCAGCCACAGA  
 AGTATCTCCAAAAAGCAAATCTGGTGACATGAAGCCCTTGCCACAAAACC  
 ATTCATTACTGGTTCCACACCTCCTTTGTGGATAAGTTCAAGCTCCTGAG  
 TGTGGCAAGCAGGGCCACCTGGAATCCCCCTGCCCTCCTCTCCTATCCCA  
 CGCATCAATCTTTCTGCTCTATTTGCAAGTTCCCTGAATGTGATATTCTTT  
 CTAGTCTCTGTGCTTTTGCAACCTGTTCTTCCCTGACTGGAACTCCTT  
 CTCCTCCTTGTAGTTTGGCTAATTTCTAGTCTTTCAAGACTCAGCTCATG  
 CTTACCCCCCTTATAACAAGTCCTTTCCCAAGCTGGGTGGTGGATGCTC  
 CTCTGTGCTGTGTGAGTCTTGAAATCCTCAGCAAACCTCAGCTTTGTTT  
 GCTTGTCTCCCTTGTCTGCTCAATGCACCTGATTACAGGGCTGGCATATACTG  
 TTCACCTCCATGACTGGCTCATGGTGGTGCTCCGTGAATATCATCCACCC  
 AAACGGATGAGAGCTACCATGCCATCACTTGTGACTTCCATCTGGAGCTA  
 ACCTCCCCCGACAGGAAAGCGTTTCTTAGGAAAGAATATCTTTGGGTTA  
 AATAGAAGTAGAGACTACCAGAAGCACTATGTCCAGCTCAGAATGAACT  
 GCTCAGTAAGCAGCCTTGTCAATGAGGAGGCAGCAGGCCAGCCCCAGAGG  
 CCTCAAAGTGGGAGAGTAGAGAAGCGCAGTTCCTGCCACAAAGGCACAGT  
 GGACACCTTGCTCCCTGGCTGGCTGGAAGCAGATGGTGTCCACCTGCTT  
 CCATGGGAATCTGCACCTTTAATAAAGTTTTATGGGACAGGAAGGTGAC  
 TGGCATTGACATTGTAACGAGGAATGGGTGGTGCCACCTTTGCTGTGTCT  
 TACCAGAAATACCTGTGGCAGGTAAATTTCTAGAGAGACCTCCCATTTTC  
 TCCCATATAGCAATTTTGAATGTTTCTGAGGGCTTTCAAATTCATCT  
 GGGAAATAGGAGTTCCAGAAAGATGAAATCAAAGGTGATGGTATGCCAA  
 AGAAAGTAGCTTTTAGAATGACTTACATTAGCCATTATCCATTACAGCAC

FIG. 3 (28 of 52)

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ACCAGGCATTGAGTTTGGAGGGGTGTGTGTGTGTGTGTGCGCGCGCGCGTGTG  
CGTGCGATGAGTGCATGCGCGCGCGTGTACATAGGGGAAGGGAAACAAAAC  
AAAAGTACACAAGACATGATAGTTGTCTCAAGGAGTTTTTGCAAATGTT  
CACAAATTTAAGAGAATATGCTGTGCTGTGGCTGGTGTATAAACCAACTGC  
TAGGGAGAGGCCCTTCCACACACACTTGGGGCAAATGCGACCTTAGGACT  
GCCAGTGGAACTCTGGGCATGCTGTTTGTGGTGCATAAACCCCTGCTCCCTT  
GATCAGGGACCTATGTTTACTTTTTCTCTCCCTGGAAGTCTTCATTAGTG  
GGCATCCAGAAGGTCTTGACAGGGCAGAGGGAGGCACAAAGACAAGAGT  
TTGAAACCAGCCTGGACAACAAAATGAGTTTCTATCTTTACAAAAAAAT  
TTTTAAAAAATAGCCAGGTAGGATTGCATGTGCCTGTAGTCCCAGCTAT  
TCAGGAAGCTGAGGCAGGAGGATTCCCTGAGACCAGGAATTTTGAGGCTG  
CAGTAGGCTATTAAGTTGGCGCAAAAGTAATCGTGGTTTTTATCATTAAA  
AGTAATGGCAAACTTTTAATGACAAAAACCGTGATTACTTTTGCACCAA  
TTTAATATGATTGCACGACTGCACTGTGCTCCAGCCTGGGCAACAGAGTG  
GGACCCCTGTACAAAAATAATAATAATAATAATAATGTAACATGTAAAAAA  
ACCCCAAAAAACAAAAAATGGGTGTTGAGACCCCTGAATTGAGGAATAA  
TAGGAAGGAGTGTGATTCTGTGTGTGCATGCATGGGTGTGCACCCTCAGT  
GCCTGGGTGGCTTACCCTGGGCTAGTTCCAGGTGGCAAATGGTTTTCTCC  
AGCTGGGCTACCACCATCTTCCCCCAGGGCCTGTCCATGTATTTGGTGGC  
AAGATACCTATGGACTAGAGTCCCTCCTCAGAGGAAAGGCTCCTCCCATT  
TCTCTGGCTTTTCAAGTAGTAGTCCATGACTTCAACAGGTCCCCAGTGCAA  
TGTTATGGGTTAGTTTAGGTGGGGTCTCCTCTGAGAGCCTCCCATAGCCC  
AAAAGGCCCTGTCTAGCTGGCACTGCATCTCCCTCTTCCCAGCTCTCAG  
CCTTTCTCTTTGCTCATCCCACTCCGCACAGGCTTTCTGCCTGATCCTTG  
GATGTGTCAATCTCTGCCCTAAGGGATGCAAGGCAATTTGTCTTTTATT  
ATTAAGATCTCTCCTGAGGCCACGTGTGGTGGCTCACACCTGTAGTCCTA  
GAACCTTTGGTAGGCCAAGGTAGGAGAATTGCTTGAGCTCAGGAGTCCAG  
GCTGTAGTGAACCATGATTGCACCATTCGATTCCAGCCTGTGTGACACAG  
CGAGACCCTGTCTTTTTTCTTTTTTTTTTGGAGACAGGGTCTCGCTCTGT  
CATCCAGGCTAGAGTGCAGCGGTGTTTTCTGCTCACTGCAGCCTCAACC  
TGCAACATTTTTTGTAGAGACGGTGTCTTGCTATGTTGCCAGAGTGGCCT  
CAAACCTCCTGGGCTCAAGAGATCTTTCCACCTCAGCCTTCCAAAGTGCTG  
GGACTACAGGCGTGAGCTACCGCGCCCAACAAAGACCCTGTCTTAAAGAG  
AAAACAAAAATAAACAACTCCCTCAAGTCTTTTTTTTTTTTTTGGAGCGG  
AGTCTCGCTCTGTGCGCCAGGCTGGAGGGCAGTGGCGCAATCTTGGCTCA  
CTGCAAGCTCTGCCTCCCGGGTTCACGCCATTCTCTTGCCTCAGCCTCCC  
GAGTAGCTGGGACTACAGGTGCCCGCCACCACGCTGGCTAATATTTTGT  
ATTTTTTAGTAGAGATGGGGTTTCACTGCGTTAGCCAGGATGGTCTTGATC  
TCCCTACCTTGTGATCCGCCCGCTCGGCCTCCCAAAGTGCTGGGATTAC  
AGGCATGAGCCACCGCGCCAGCCAGACCTCTTGAGTCTTAAACTCCTCT  
GTAGTTCCAGCCACCCTTTAGCACATGACTCTGTTAATTTTGTCTCACT  
GTCTGAAATCATCTCCTGTCCACTCTTGACTGACAGGTCTCTGCACTAGC  
CCACTGCTTAATCAGAGTAGGTCCCTGTCAACTTATTCATATTGTGTCCC  
CATCTCCTTCCAAGTCTCTCACTTGCTGGCTCCTGTCTTAGTTTTAGTCC  
CCATTCTTCAAAGAACGTGAGCCCTGGAAAGTATTTTAGTCATTTAGTTC  
AGTGCCTTTGGATGGGAGGATCACATCCCTGGGTCCCGTCTCTGCAGACTG  
TTTTGCTCTAGCTGACTAGGCAGGATTCCCTGCCTTCTCTCACTTCGGCA  
TGGGACTTCTTCTGAAATTGCTGCTCAGTCAAGAGAATGACCTTCCCCA  
ACATAATCCTACTCCACAGGGACTTAAAGGTGTGTGAGAGATCTCTTGCT  
CATCTTTCTGGCCAGGTGCCAACGTCAAGTTATAGCCAAGGGACAAGACT  
AGTTAGCAGATCAGGCAGGTCTTAGACCCCAAGCGTAAGTGCCAGACTTCT  
AGCTGCAGTTGTTCTGCCCACTGGGCGTTCAAGTGGAGAGAGGGCAT  
GGCACTACACTGAGCTCTCGGCGAAACCCAGGACTCTGAAATCTCGGTGT  
CAGCCACAGGCCACTCTTTTCAGCAGGACTTCAGTCAGTCTCTGCTACTAG  
GCTGTGAGCACATGGTAGGCTTTACCCC

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AAGGAGTGTGCTTGCTGATAGCATGTGTGANGGGACGAGGAGTAAATAAT  
TTCTGCCTTCAAGAAATTGCAAACTAGTAATGGAGATAAAATCAACAGAG  
GAACAAATTAGAGTATAAGGTAAAATCTAAGGGCCATAAGAGAGGAGAAGA



AGTATGGGAGTTGAGAGGAGGGGGTAAATGAGGGGAGTAGGTGGGTAGA  
AAAGGTTAAAAGTAAATAATGATGGGAAGGAAGACAAAAAGACGACAGGG  
GTGCCAAAGGACTCTTAACCTCATCTGAACGGAGTTGCCCTGTTTTGCTC  
TCTGATGCTCATGTATCTATCCTTAGAGACAGCTTGGCGGGCAATGTAGA  
GCGTAGGGGCTGACATAGGGGGTGGAGTCCACCTCCGTGACTTCTAGC  
AAATTAGCAAACCTTTGCTGCTGCTAAGCCTATAAGGCGGACAGAAATGCC  
ATCTTTAAAGCTTGTTATGTAAAGTGCTTAGGACCTCGTAGGCATCAACA  
GGAATAATGGATGAAACAAAAACAACGGTGCGTATCTTGGAGAAAGTGGCA  
TCTGAGCAGGAGTATTTTGAAAGGTAGGAAAGGGCTCCAAGCACATCTAA  
GAGATTAGGGAACGAGAAGCCTTAGCCCTGGGTGCAGATTTAACCAATC  
AATTTCTAACCCACCGCAGGCTGAGAGGTGTGGAGTGAGAGCCCCGCCAGA  
GGCAGGAGACCCGGGCTTCGGCCAGACCCCGCCTCCTGGTACAGAGACC  
ACGCCCGGCTCTGCCTGGAGCCAAATGTGGATCAAAACAGCGCGCAGCTT  
CCCCTGCTGGTGAACCCGAGCAAGGGGCTCAGTTTCTTTATCCGGA  
ACGTGGTGACAATGACATCTCTTTGCAAGGCTGCTGCAGGGCTTTCTGGA  
AATACGCCCGTGAGGTATCTGGGCTGCGCACAGCCTCCCCCGCCAGGA  
CCCAGACGTCTACCTGGGGGTCCCGTCTGCGCTCCCGGGATGGAACCGC  
CCAGGGGAAACTTAGGCAGGCGAGCGGACGGGCACCTCCCGCGGACGAA  
CTCACTCGGTGGCCTCCTACTTCCCGCGCGTGTTCACACGCTGAGAAT  
AACGGGAACAGCGGTGCTACTCACCGACAGCGGCAGCAGCGGTAGGCCCG  
GGCCCCACCATGACTCTTCAGTGACAGTTTTCTTCAAACGCCGCSCTG  
TAGCCAGGACCGCGTGCCGCGCGTCCACGCGTCTCATTGGCTCCTGCG  
GTTTTGAAACTCGCTAGTCGTGACACGGGAGGGCGGGAACAACAGGCAAT  
AGGCTCTTTGCGGTGGCTCTGGCCTTGAGAACCCGACCTTGGGGCCCTT  
TGATTGGAAGACGTGCAGCGCACCTCGGCATTGAGGGCGGCTTCTCGG  
GGCGCGGCGCGCCCGCTCTGAGTGCGCCTGTGAGTGCGCCTCCGAGTG  
GGCGTGGGACCCTCCGTGGGGGCTCAGCCGGGCTGGTGGTTGGGGGCG  
GTTACGCTGAATCCAGCTGGGGTGGCGCGCGGGAGTCCCTGGGCGGAG  
AGACAGGGCGGTCTCCAGGATGCTGGGGCGCTACCTGATTCTGTCTCT  
TTCAAAGTCTCAGACTCACAGGAGCTGTGAAAAATAATATTATAAGAG  
GACATATGGGTCTTATGCATCTAAAGGCTCTAGTTCTTAGTACTGCAGG  
GTGGCTCGTTTTAATTGTGGTAAATATGCATAACATCACATATACCATT  
TAACCATTTTAAAGTGTTAAATTTTCAAATGTGCAGTTTAGTGGTAT  
TAAGTACCCTCACATTGTGGCACAGCCACCACTACTGTCTTTCCAGAAC  
TTTTTCATCTTCCCAAATGAAACCCGTGACCCGTCACTAACTCCGCACTC  
CTCCCTCCCCCAGCCCCAGGCAATCACCATTCTAGTTTCTGTCTCTATGG  
ATTTGACAACCTGTAGGTGCCATATAAGTAGAATCATGCAGTATTTGTTCT  
GTGACTGGCTTGTTCCTTAGCATAAAGTATTCAAGGTTTATCCATGTG  
TAGCATGTGTGAGAAATTTCTTTCTTTAAGGGGAATAGCATTTCGTT  
GTGTGGAGATGCCACATTTTGCTTCTTGGTCCATCCCTCTCCGGACACTT  
GAGTTGCTTCCACTTTTTGGCTATTGTGAATAATAATATGAACATGAATG  
CACAAATAACTCTTTGAGACTCTCTTTTCACTTTTGGGTATATACCA  
CGAAGTGGTATTGTTGGATCAAACGGCAATTCTATTTTTAATTTTTTGAG  
AAACTGCCCTTACTCCTCTCACGGTGATCTCTGTTCAAGGTATATTTTCG  
ATTTACCTGATCAGCTGACTATAAGGCCATAAGGCTAACGGAGAAACGC  
AGGCCTAGTTTCTCCTAGTTACTAGGAGATCGCAGGCCTCGTTGCTCTGA  
ATCCCTAGACACACTTCATCCCCCTTGTTTAATCCTAAATTTTTTTCT  
TTTGAAGTTTGCTCTGTTTCATCTATTCTCCAGTTTCTTAAAGAGGTCTG  
GAAAATGCTTTGGCTCCTTGTGTATGAAGTTTCTCTCCATGGATGCT  
GGAGAAGTCGTGTGTGGAGGGGAGTCATATCTGGGCACCTGTTGGCCAG  
GTTGAGCTTACCAGTTGGGTACTCAGCAGGGCATGAAGCCACTGCAGCAG  
CCCTTCTCTTAGCCGTAAATAGGGAGTTTGAAGAGAGCCAGGGTTTCT  
GGATTTATGCATTTTGATATTTCAATAGTGTATTAAATGTTTAAATAG  
GAAACTGATCATTATTTTGTAAATGACTGAGAAAGGGACTCCTTCACC  
AACAGTTTCAGAAAAGTGAAGGCGTTTTGTTTTGGTCTTTGTAGAATCT  
AGGTGGTTGAATGCATGTGAGTTGTAGAAGTCACCTTGCCGTGATATCCCA  
CGCAGTGCTGGAGTATTCACAGACCCCATGTAGGTACTGCACCTTTGCA  
GGTATACTGCTGGTGTGGTGAGCTGCCTTACCTGTCTGTTATTGGAGA  
CCCCGCTTATTAGGAAACTTAAATGAACTCAAATGAGCTTCTTGCTT  
ACTGGTCTAGTCTTTGGAGCAACATAGGCCAGTTCTGCCTCGTTTTTT

FIG. 3 (30 of 52)

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TCCATCCCTTTGGGTATTTGACGGTCTATTTTGTAGGACACAAAATGTGGG  
AAAAATAGCTAGGCAGGTTTAAAAATCTCAACTCTACCAAGCATGGTGGC  
TTATGTCTGTAATCAATCCCAGCACTTTGTGAAGCTGAGGCAAGAGGATT  
GCTTGAGCCTAGGAGTTTGAGACCAGACTGGGCAACATAGCAAGACCTCG  
TTTCTTAAAAAATAAATAAATAAATAAATAAATAAATAAATAAATAAATAA  
CACACCTGTAGTCCCTTCTACTCAGGAGGCTGAGGTGGGAGGATCACTTG  
AGCCCAAAAGTTGAAGGATGCAGTGCACCTGTGGTCATGCCACCGCACTCC  
AGCATGGGAGGCAGAGCAAGACCCTGTCTCCAAATAAATAAATAAATAA  
ATTCTTAACTCATTATCAAAAGTATCCACTGTAGCTTTCCATCATCTGG  
TGT  
GGCATGTATCTCAGCTCACTGCAGCCCCACCTCTCTGGCTTAAGCGATCA  
CCCACCTTCAGTCACCCATCTGGGTAATTTTGTATTTTGTAGAGATGG  
GGTTTTGCCATGTTGCCCCAGGTTGGTCTTGAACCTCTGGCTCAAGCGAT  
CCATCTGCCTCCATCTCCTAAAGTGTGGGATTACAGGTGTGAGCCACCA  
CACCAGGACAATCCTGGTGGCTTTTAAACGGTTTTCCATTGCTCTCAGCT  
AATGACCTATAAGCCCCCTGCGGGCTTGGCCTTTTACTCCCTGAGCATTAG  
CCACCTCCCTTAGCCTTAGCCCACTACTCTCCCTTGCTCAGTGTAT  
CCAGACACTTTGTTTTTCTTTTCCATCTCTCTGTCTGGGAATCCA  
ACCTTTCTCTCATTTCTCTAGTTGATTATTATTATTTTACTCTAGCA  
GCCTTATTGAGATATTTACATACCGTACGATTCTCCCACTTACAGTGTAC  
AATTCAATTTTCTAACAATTTTCTACCCCTTAAAGAAACCTTACTCA  
TTAGCAGTCACTCCCAATTTCTCCCTCTCTCAGCCCTAGAAACCATGA  
ATCTACTATCCATCTCTATAGATTTGCCTCTCTGGACATTTTATATGTATG  
AAATTTGCAATTTGTGGTCTCTGATGGGCTTCTTTTGTACCAAAATAT  
CATGGGTTTGATCTAGGTCCTGCTGCTCGCTGCACAGAAAGCCAGCCACT  
GAGATGACAAGTATTGCCAAGGAAGAAGGCTTTAGTCAGGTGCTGCAGCT  
GAGGAGATGGGGGCTCAATCTCAAATCCATCTCGCTGACCTAAAACAGG  
GGTTTGGATAGCAGGGAAGAAATGTAACAATGCGTAAGAAAACAGGAACC  
AGGGAGGGGCAAGGAAGCAATCCTGATGAATGAGTGGTCCAAAGTCTCAT  
TGCCTGGATGTGGTGTCTGGCGAGTTTCAGTTCTTTGATACTTTTTTTG  
AGAGGCCTGAAGTCTTTTCCCAGGAAGGAACCTCAAACAAAACAAATACA  
AGCTTCCAGCTTTAAGACCAGAAGCGTCAATTTCTATGTTTATCCGAAAG  
AACAGTCTATGGGACTATTGGTTAAGTTTCACTTTCACTTAGTATGCTGT  
TTTCAAGGTTTATCCACATAGCATGTGTGAGTACTTCACTTTTATGAC  
TGGGTATTCTATTGTGCGGATATACAATATTTTATTTGCCATTATCAGT  
TGATGGACATCTAGGTTCTTTCCACTTTTGGCTATTATGAATAATGCTG  
TTATGAACCTTTATGTATAAGTTTGTGTAGACATATGTTTTCAACACT  
CATGGGTATATACCTAATGAGAGGAATTACTGTGTACATACGATAATTCTA  
TCTTTAACCATTGAGGAACTGCCAGACTGTTTTCCAAAGCAGCTGCAGC  
ATTTTACATTTCTACCAGCAGTGTATGAAAGTTCCAGTTCTTTACATCC  
TCAACAACACTTGTATTGTCCATCTTTTAAATTACAACCATCCTAGTGG  
TTGTGAAATGGTATCATTGTGGTTTTTATTTGTATTTCTTGATGACT  
AATGATGTTAAGCATCTTTTATGTGTTTACTGGCCATTTGTATATCTCT  
ATTCAGAGTCTTTGCCAATTTTAAATTGGGTCAGTTGTCTTCTTCCCTT  
TTTTTTGAGATGGAGCCTCACTCTGTTTCCCAGCTGGAATACAGTGGTGT  
GATCTCAGCTCACTGCAACTTCCACCTCTGTGTTCAAGTGATTCTGGTG  
CCTCAGCCTCCCAAGTAGCTGGGATTACACGCACCTGCCACCATTTCCAG  
CTAATTTTTTTCTTTGTATTTTGTAGTAGAGACGGGGTTTACCATGTTGG  
CCAGGCTAGTCTCTTTGTGACTCTTAACCATCTTCACTCTCAGACAAA  
ACATCCCTTTCTCAAGGATTGTGATTAGCTTGATTATTTGCTTATCTTTC  
TCCCTGCTAGTCTGTAACTGAGGGTAGGCCACTATATTCAATTGTTCTTG  
GCACCAATAGAACTAAATTAATGTCTTTTGAATGAATAGGGCTTTCTC  
CTTTTAAAGATCCCTTCAATACAGTAACCACTATATATAAGTAGCCAC  
AAGCCCATTTCAATAATACTACTAGTNCCTTGCGCCAAACC

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GGCTCAGCGTTACTATACTGGTCTCAAACCTCCTGGGCTCAAGCGATCTGC  
CCCCCTCGGCTTCCCAAAGTGTGGGATTATAGGCGTGAGCCACGGTGCC  
TGGCCTCAAATAACTATTTAAGTGAAACAAAACCTAGTATGGCACTAATGA  
AAAATGTATAAATCCATAATCGCAGAGGGATTTCAACTTACTTCTTTTGA  
TTATGTAAAGGTCAAACAGACAAAAGACAATGACAAAACCTAATGCAATG

FIG. 3 (31 of 52)

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AACACTTTTGATTTAATGAACATATATTGGATATGTACCCAAGAATTAGA  
GAATACATACTAGTTTTGAGTTTATGCAGAACATTTACAAAAATTTAGTG  
GAAGCCTAAATTATAAAAAGTTGCTGTACGTTAGTAATAACACACAAACCC  
TTGAGTCCGGAATTCAAAGCCCTCCACACTCTCCTCTACCTTTGCATCTT  
TATCCTCCACCACACTGCAGTGCATACTCTGGGCTACTACTCACTGTTCT  
TGATTCAAATTCATGTTCTGTGCTCAGCTCAAATCATTCTCTCTGCTGGAA  
TAAGTACTTTCATACATATTCTGCTATTGAATTCTTGTCTTAGCACCCCAT  
CTACTCCAAGACGATGTCCAGTTGGGGTTACTCCCTGTCCCATTTTCTTT  
GATTACACTTTTTTTTTTCTACTTCCATTATATTATTGATCACATCTGTGC  
CACAGTTTTTGACTTTGTGTCTGCTTTTACTCTTTTCTAGACCCCTGATAG  
CTCCTGAAGGGTTGGGTCAATTTCTTTTTTATTTGCTCATTCTCATGGCA  
CAGTGAGTGCTTAATAAATGGCTATTGACTGAAATTAAGTATCTAAA  
TGGACATATTCACCTTCTGGGCCATTCAATCTTTCTTTCTATTGGAACCA  
GGAGATGGGGAACCATAAACAAAGGTAAGGTTGTGCCATGTGAAAGAAT  
GGAACCTTCCCTGAGGGCCAAAAAGAGCAGGGAAAGGTGCAAAGACAA  
AATCTTCCATTTTAAACAATGTAAGAATGTGGTCCACCTCATGCTCAGG  
TGGGACTTTATCATGACGTTATTTTGGGGACTTATAGCTGCATCATTTA  
CCCCATATACATTTTACCTTTAGTGTAGGGAAGTGAAGACAGGAATTTGT  
TGATGCAGACTCTTGCTAATGAGGCTAACACTTGGAGAATTTTATCATG  
CATTCAAGAAGCTTGTTTTACATTTCTTCATTAATACTTTAGTTGGTGGT  
TTAGCTTTAGTTGTAGGCTTATCAGATATTTGGAGATATCTTCATRAACG  
ATGGCTTTGGTTTTAGAAGAGTTATTCTGAAGCTACTATTTCTGGCAATA  
ATCAAACAGCATGGCCATTTGTTTTGTAAGGCCTTCTCTAGAATATGACG  
GTAAATCTACGTGTGGAAAAATGCTTATTCTCTGTCTCTATAAATGT  
GAATCTAGTTTGTCTTCAAATGAAATCAAGTGATTAAATGTAGTTTTC  
TAAGAAGATAAATGGAGCAAAGCACTCTGTGTTTTACAGTGTTGGAAATC  
ACTCATCCCTCATAAAAGTGTCCCACTGATCCTGACTCATGAATGAA  
TTAAATAAGAGTTAATAACATCAATTTACATTTTAAAGACACTTTCCC  
ATGTTTTAGACTATTGGTTGGAAAAGCTGGTAGGTGTACAATTTGTGGAG  
AGTTGGCTGTTTTTGTCTGTCTGTTGTTGACGTATTTCAAAGCCATATCT  
AATTTTGTGTGCAAGTGGTCTGAATTTACAAAAATGTTGAGTTGTGTAG  
TGTGGAGAAGTACGGAGCCATTTACTGAAAGGCTGGGGGAAATGACGAG  
ACCCTGAGATAAGGCAGTAGTGGTGCGAACAGAGTGGAAGGGAGGTAGTT  
GAGATATGTTGAGAGTAGAATCAGAATGGACATAGTGAACAAGTGGATGC  
AGGTGGGGGCTGAGGAAGCAAAGTTGAGGATAATTCTGAGACTTCTAGGT  
TGATCCACTGAAGTTACATTTATCAACACCACAAGGAACTAGGGGAATG  
AGAAGGCATCTGTTTTGCTTTGGAGTGAAGGGCAGTGATGTAAGAGGA  
CTTAATCAGTTAAAGTTTGATATGCCTGAACCTCAATTTGATATGTGCA  
TCTGATATACCTTTGGGGTGACCTCCAGGCAATGGTTGAACATGTGTAT  
TTCTTAGTAAGTATAGGCATCACAGACTCACATCAGTAAGGAAGCAACA  
GCAAACTTGATTGGACGATATACCTGGAAGTCACTACCCTATGACTGGAG  
CAAGTCTCTGTGCTGAAATGAGGATAAGAAGAATCTTGACCTTGTGGAA  
TATGTTGTTAGGAATATATGTGATGAACAACATAGGATACTTCTACAGG  
GCTCCACATGTAGTAAGGGCTTTATAAATGCTTGATAAATATTATTGTTG  
TAATTTATTTCCAAAGTAAGATGCCACTGGAGGAATCTTTGGAACCCAAA  
TTAATAACAAATAGGACTGGATGCAATGGCTCACACCTGTAATCCCAGCA  
CTTTGGAAGGCCAAGGCAGGAGGATCTCTTGAGCCCAGAAATCAAGACC  
AGCCTGGGTGACACAGGGAGACCTTGTATCTATGAAGAATTAATAAAT  
TAACCAGATGTGGTGGTGACGCCCTATAGTCCCTGCTGCTTGAGAGGCTG  
AGGTGGGAGGATGCTTGAGCCCATGAGGTTGAGGCTGCAGTGAGCCATA  
ATTGTGCCACCACACTCCAGACTGGGTGACAGAGTGAGACCTTATCTCAA  
ATAAATAAATAAATAAATAAATAAATAAGTACAAACCAGCAACACTAAT  
CCTTTCTAGAGATTATTGAACTCTGGAGGGCAGATCTGAATGGAGCCAGC  
AGAGGGACCTATGAGAGATCAGCCTGGCCCTGGACAGCACCAGGCAATGGG  
GTTGCTAGAGAGGTAATGGGGTTGAACAGGGTTTAAGCCATGAGGTCTCA  
AGAATCCGTGAAGACTCAGACTAATTTTTTTTTTTTTTGCATGAGGATTAG  
GTGTTCTAGGAATTTCAATGAGAGCAGGTTAATGAAGGAATGCAGGGT  
AGGAGAGCTGAGGGAAGGCATCTGAGAGAGCCTGGCTTATGAATGGCTGC  
CTCAGTATGGCTCACCTGCTTCTCTGTATCTACTTAGCAGATGATCCCA  
CCCCAGGCCCTCAGGGCCAAGGTCAATTTCCACATAGTCATGGGCCCTTGA

FIG. 3 (32 of 52)

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GGGCCCTGGAGCAGTGTAAAGGAAGACAGAGTCTTAAGAAATTGCATTAAAC.  
BTTCATGGTGGCTTGGCAAGTGTGCTCATCCTATGCCAAGCCTGATCTGAAG  
GGGTGCATGCTCATAGGTAGCTGCTGCCCAAGATTACAGCAGCTTCTTCA  
ATCCCAGATCCATGCTCTCCTATATTCAATTTTCCAGGGGTTCCTGTCTCT  
TCGACAGTGTATGAGATGCAGAATGACTTATTGAGTTATTCTCCTGATAGT  
TGCCCACTTTTCCAAATGACAATGGGGCATGGAGCTTGAGAGTGGAATG  
AGGCCCTAGGGATAGCGTGCTTAGGAAAACACTCCCAGCCTGATGTAATT  
CTGGGGGTACAATGGCATTTTCATCATCAAGACTGATGTAAAGGGTGACT  
AGCAGTGAGTTGGGGGTGACTCGCACTGGGGCTAGGTTTCTGATTCTGCC  
TAATCCAGACAGAGCAGAAGCACTAGTGGGCTGGTAGAGGGCTCCAGGG  
CCTCACTTAATGTCTTGGAAAAACAGCTCCAGATTGTTGGTTTACGTTCT  
GAGGACAAGCTTGGGTACTACAGGATAGAGAGAGTGGTGGGAGATGCCGT  
GGCCTGCCCTGTGATGCCCTGCCCTGCCATTCTGCGTGTGATGTCTCTG  
GGGCATCTTGCCTTCCCTGCCAGACCTGTAGTTCAGCTGAGGGCATGTG  
GAGGCCAAATGGCTTCTTAGAGTGTACTTTCTTGAACAGCTCTGCTGG  
GAGAACTGGAGGAGCTAGCTAGTCACGGTAACTGCAGCAGTCAAAGGATC  
GTCCCGGTGGAGGTGGGGTGGAAAGGTAGAGAAAGAGAACATATAGCGTT  
TTCCTTGGAGATGTGTGGGCATGTCTAGAGGAAATACCCAATTCCTGAG  
CCTTGAGCCCTCCAGGAAACCTTGGAAATATTAGGTTAGTCATCCCCAAGG  
AAGTCTAAGAATTCTGGTCTCACCCTCTCCTTTAATTCCCAATGATC  
CTACATGATATTAAAGGAACACGGGCCAGTAACCTCCAAGCAATGGATGT  
GGTGGTGAAGTTTGACCTCATGATGGAGCGGAGGTTGGTTTGAACCTAA  
CAATTTAATTTATTGTTTCAAACCTGTTCTCCACTCAGCGTTATTAAAGCA  
TACATAATTGACACATAAAAAATTGTATATGTCTACGGTGTACAATGTGAT  
GTTTGGATCTATGTATACATTGTGAAATGATTACAACAAGCTAAATAACA  
TACCCATTCTCGTGTCTCAAAGGAATTAAGCTCAAGCACAAAAGAGAGG  
TGCTGTTGAAGGTAGGGCTGCTCTATCTAAGTAGTATGTCTGGGGTGT  
CCTGGATCAGGGTCTTTTGTGCTAGTAATAAACAGCCCTTCTGGGGCT  
GCTCCACTTTCCCCACATTTTCTTCTGGAGCCTCCCTAAGAAATTAGGACA  
TGGCCACTTTCTCTGCATAGGCTTCTACTTCAACAAGGACAGGGCTTGT  
GCTGCCCATGCCACTTGAGTGTCCCTACAGCACAGAGCTGAGTGCACAC  
TGGCTGAGTGAGGAAATCCCCAGATTAATCTTGGTTCTAAGCATCATGG  
CTGTATTTTACACGTATATGAATTACAAATTACAGCATAGTCAATAAGG  
ATTTTTGTGCTACAACCTGGAATCCCAGATTATGCAAATTGGATAGTATAA  
TATTGAAATTCCTAGGACTTTTTATTAGTTTTAAAAAATTATACAAGCTT  
AGAGTAAGAAATTAACAGTGCAAAAGAAATTCAGTGTGAAAAGTAAATG  
CTCTGTCTCTGCTGAGAGACAGATATTGCAGCCAGATACTACTGGGGTC  
AATAGTTTCTTAAAGCATGCCATTTTGATGGTTTATGGGACTTACAGCT  
CAAGAAGCTTGACACTAGGGTTGATCTCAGAAAATCATTGTTGCAGGTAT  
TAGATATGACCGTCTCATAAAGATACACACACAGACACAGCGATTGGAGA  
TATTCACTGGGGCTTATGGGCTGCTTGTCTTTCTGCTCTGTGCCTAAGT  
TGGGCTCAGAGTAGCCTGGCATCGGCTGTGGGGAGAATGCTGGCATGGGG  
TTAGCAGGAGCCCACTTAACATGTCTAAGCCACCTGGAAGAGTCTTCA  
AGGAGACCAGACTCCAGAGGCCCTAAGGAAGGAAGGACTTTTGGCCGTTT  
TTAGGTATTCTAGTCCCAGAGTTTAGGGAGGAATGGTTTGGCTTTGGGTC  
TGTGCCCCCTTTACCGAGTGGGATGGGATGTGCCCATGAGCTGTTGAGCT  
GGCTCTTGAGAGAAGACAGCAAAGCGGGAATAAGAGGTCAAGGAAGCTGTG  
TGGTTGTAGGAAATCCCAGCAGAGGGCTGGGGGTCAAAGTGGTCATGG  
TAGTGACGGTGGAGGCTGAGGTGGTAGAAATCAGAGGACAAACCCATG  
GGCTGCTGGTGTATCTGACCGAGCTCCTATGCTCTCCTGGTTCATTTTAGG  
CTCTGTAGCAGCAGATGATTGGCTGGTGTGAGAGCAGTGCACCTGCCATA  
TCAGGCAATCCAAGACAAGTCCAAGCTACGCTGGGAGGAAACCTGAAGGC  
AGCAGCAGGTAGACTGGCTGAAGACAGACAGGCAGGCAACTTGTCAATCA  
GATTTGTGTTTTTAAGGACTTTTAACTGGGGAGCCCTCCGGGACAGATCA  
GATGAGAGTGAAATGTGCTCCGCCTTAGCC

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GGCCGTTCCCAATTCTGTAAAGGGAGAGTGGTTTTATTTATTTTAAAC  
ATAGTCAAGCTGCTAAAGTATATGATATGTATAGATAGAGTATAATTAAA  
TACTTTCACTACAGACAAAATCAGGAGAATGGAATTAATAAACAATTTA  
CAAATGGGTAAATGGCAGCATTGGGTTGCGCCCAACCCAGAGAAGGCAGAC

FIG. 3 (33 of 52)

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ACCAAGATTCTAAGATCAACGTTGGCCAGCACCTTCAGACTTCAAATAGAA  
TTCGTGATTATGCAATTATTTTTCTCGGAAAGTTTTCACTTCACTATATGC  
TACTTGACACTTGCTTTCTTAAGACATCCCTCTATTTTTGAGATGACTAA  
TTCAGCAATTCAATTTCTCTCACGCATAAGCTGTCACTCAACCCAAACCCA  
CCAAGCCTGCAATCTACCTCAATAAGGTCTTGGTGTGTAAACTGACCCA  
CTTCACCTAGTTCTCTAGCCCTCTCTTGACCAGACATGACTCTTTCATAA  
CTAGACCTATAAAGTCAGGGCTCTTAAGTAGCTGATCTCTGATAGTGCC  
AAGTGTCCCCCACTGTTCAATTTTTCCACTCCAGCTTCTAACAGGTGATA  
GACTGCTTTTTGGGGGTAGGGGCACCAAAACATATAGACCTCATGTTTGG  
ATGTAGACACTCCAGTTTCTTTAAATTACAACTACATATTAATAAGTACT  
TCCAAGTGTACATTTCACTCCAGATCTCTCCCTGGATCCCCAAACTTTGT  
AAAACCCACCGCCTAGTTGATATCTTTGATGTCTGACAGGCATTTCAA  
TTTAATACTGTCAAAACAAAGTTATTGATTTTCATCTCTGCATCTGTGA  
CAAATTTTTCTTACTTTGGTAAATAGCACCCAGGCTGTGTCACTGCCAA  
GAACTTTCCACAGCTCTTGGAAATAAAATTCAAATATTTTCCAAGGCAGA  
AAGGCACAGTGTAACTCTGGCTCTGCTACCTCTCAACCTCGTATCACA  
CTAGTCTCCCTGTCACTCACCCCTCCAGGAGCTCAGGTATCTTTAAAGT  
TTCTTTTCTTTTTTTTTTTTTTTTTTTTTTGAACAGTTTGTCTGTGTT  
GCCCAGGCTGGAGTGAAGTGGCATGATCTCAGGTCACTGCAACCTCCGCC  
TCTTGGGTTCAAGTGATCTTGTGCTCAGCCTCCCAAGTAGCTGCAATT  
ACAGGCGCGTGCCACCACCCGGCTAATTTTTGTATTTTTAGTAGAGAT  
GGGGTTTCACAATGTTGGCTAAACCGGTCTCAAACCTCTGACCTCAAGTG  
ATCTGACCACTTCAGCCTCCCAAGGTGCTGGGATTACAGGCGTGAACCAT  
TGTACCTCTCCTCTTGAAGTTTCTTGATCCAGACTCATTCTGCTTAA  
GGTCTTGCATCTTCAGTCTCTCCCTCAAATGACACCTCCATGAAGACGCA  
ATTACCTGTAATTACCGTGTCTTATTAGTCAATGTGTTGGTTTTCTGTC  
TCTCCACTACAGTGTAAAGCTCTATGAAGGCAGAAACCTTGGCAGTCCAG  
TTCCAGCACAGTGCCTAGCACACATAGGTATTTAATAACACACAGTAAA  
ATTCACCTTTTAGTGTGCAATTCTGAGTTTGAACAATGCATCAAGTCAT  
TTAAGTCTGACTATTATCAAGCTATAAGATGGTTGCAACACTATCACTAA  
TTCCCTCATGCTCCTTGGTAGTCAGTCTCACCCCTAACGCCCCCTCTG  
GCAATCACTGATCCGTTTTTGTCTTTATAGTTTTGGTTTTTCCAGAATG  
CCAATAACTAAGTTTTGAATGAATGAATGCTATTAACCTCTCATTCTGAC  
TCCAGAGCAACATCCATGCAATATTTATTATTTAGCCCCAAATACTGCC  
CCCTCACCTTCACTCCAACCACCTACTTGATGATACAAGGTGAGACATTT  
GGCATGTGCTTCTCATGTTCTTAGCATTTTCCCTATCTCCTTAGCCTT  
CCTTCTAATCATAAACGAAGAGTGAACCTTCCCTTTCTAAAGGCAACTTA  
CTCCTAGGACCTCGATGCCATAATTTGTTTCTCTAGTACTTTCTATATA  
TACACCAACAATTAGCTCCAGAAAGGTAAGACTCACTGTGTGCTCATC  
ACTGTGTCTCTAGCGCCTGGCACACTGCAGGTGCTGAAGAAACACCTAC  
AGAATGAGTGAATGAATCTCTCCCTCTCTAGACTCCTTCTCTTTTGTAA  
CAAACATGTTCAACCTGCAACACAGTCTTATGACCAATCCTCTGTTGTCT  
GACCTAGGCTGAGCTCCAGGGCTGGGACCCTGACTTCTTATTACCACC  
TCAAGGTCTCTGCACTCACTTCTCTTTCTGCTCAGGATTGTTTTCTTCT  
TGTCAACAGTCTTTTCTCAGACTTAGGTCTCAGCTCAGACATTGCTGTTG  
AAAGTACTTCTACTGATCCTTTTATCTAAAGCAGCCATTCCAGCCCTACT  
CTCTTGATCATAGCACCTGAATTAAGTTGTTTACTTACTGTCTCTTTCAG  
GAGGGCAAGGAGCTTGGTGGTGGTGTTCAGGGCTGTACCAAGCTGTACCT  
TGCTTCAACCTGCTACACTTTTTAGCAACCATCTAATTTTACATGCTCCC  
TTCACTCGTCAGAAATTTCTTATTTTCTACTTCAAGCAGGTATACATAT  
GTGCTTCTCCTGGGAGGCTCACCACTTCATGAGACTACATTTGGTCTCTG  
GGTAGAAAGTGTACAAAATCCACTGGCTCAGTTTTAATCAATGTATGTTA  
ATATTAACCAACCTGAGATCTTGATTTCCACGCCTGGCTAATTTTGTATT  
TTTAGTAAAAACAGGGTTTCTCCATGTTGGTCAGGCTGGTCTCGAACTCC  
CGACCTCAGGTGATCCGCTCACCTCGGCCTCCCAAAGTGTCTGGGACTACA  
GGCATGAGCCAGCGTGCCCGGCTAAGATCTTGATTTCTACCATCTGAAC  
TCTGTATTTGAACGACTGCTCTGCTTGAGCTTACTGGCCAAAACCTTGG  
CCCACCTCAGACTCAGGGAAGTTTCTGGTTCTTCCCTGGTAACTTTTCTGA  
ACTTAACCACTGGTTTTGCTTGACAAGAGATTACCATCTTCTCACTTCCTA  
GCTATGTGAACCTCACTTATCTGCTCTATTGCTGTTCACTCTAGCACGGCA

FIG. 3 (34 of 52)

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CTTATTGAACGAGTGTCTACATCTGCACCCCTACTTCTTACTCATCCAT  
TCTGTTTCAATTTCTTAAAGAAAAAAGCTATTGTAAACATACG  
ATTACAGAAAATGATTTATAACATGTGTATGTACCACCTAGCCCTGTCAA  
GTCTTAATATTTGTTATATTTGCTTCAAATCTTTTTTTCAGACTGTAGTTA  
AAAATTACTTAGGAGCCATTATTTATGGCCTATTTCTGACCTAGTCTTC  
TTGATGGTCAATTTGCCTAATCATCTTAAGTTGCAAAAGCTTAGAATTAA  
AGCAAAAGTACCTTCGATCCTCTGCTGTTGCCCTCTTTTTTAAATATTTGGGT  
TTGTTTGGGTCCCATTTACGGTTGTGACATCAGCTTGAGTTTGGGAGCT  
GTCTTTGTTTCAGAAAATGTTTCTGGGGAACAGCCTTTTTCAACTTGGAGTC  
CAAAAGTCTGTGCTTTTTGCTGAAAGCCATTATTGTTATGTTTATTACCAC  
TGGTTCCTATTTGGTCTTATGCTAGGGGTGCTTGAATGGCTGAATTAAAT  
CTGCCAACTGTCAAATTAGGCCTCTGGCTTACGGCTTTTGACTTTTGCAG  
TACACATGATGTCTGAGGTATACAACTTGGCTGGACTTCTGATCTTGCT  
TGATGTTTGGATGTCTGTTGTTATATTACCCTGAAGCAAACTGGGGTAT  
GTTCTGGGTTTGGTGTGCTTCACTCTCTGTTTCACTAACAGGGTATGACCG  
TATCTTAGTTTTCAATTTGGTCTTTTCAATTGACTCTTATTAACCTTTATAT  
CTTTGATGTTCTTGACTACTGGTTTCTTTGATGACTGAACCTTTACTAAGG  
GTCCGAATAAAGTGAGAGGGAACCGTCTTTGAGGGTTTTACTCCTGGTCT  
TGCAAGATCTGCTCCTCTAGAGAGTTGCTGTGATTTTACTGGGAAAGTCC  
TGCTTTTGTGTTTCTCCAACAAATGTTTATTAACCTATCTTTCAGAAAC  
GCACTATTAACCTGAACCTTTGCCAAGGCTTGTGTTAGGAACTAACTGTT  
CTTGGTTTTGATTATAAGAGTCAGTCTTTGGCTTACTTCTGGTATATAATT  
TAGGATCTGGCTTCTCTCAGGTTCTGTTAAGATATCTAGCAAGTTCTCT  
TTGTTTGTGTTTCTTTAGAAAGTTATCCAAAGATCTGTTTCAACATGGAT  
ATTATTCTATAAAGTCTATACATTTACCATTTCTTGATCTGTTAAGTCT  
GCTTTGTAGTTTTCAATTGCTCTATATTAAGTGACCCACAGGTTTTCTT  
GACAGTCTCTCTGTGGTGGACTATCTAGCTTCACTGTTGAAAACCTCTT  
GCTGAAAAGCTTTAGACTATGGGTTAGAAGAAACACATTTTGAAGTCCGCC  
TTTTGCCCAGAAGTTTTGGTGGCTCTAACTTCACTTCTGGGACCCTGCA  
GTATTAGGTGGTCTGGGCTGGAGTTTAAATGCTGATGGACCTTTTAGGTTT  
GACAGGCAAAACAACATGGTTGGTAACATCATTTTTGGGTCTAATAGTCT  
GAAAAACAAGAAAATACATATTAATAAATCCTTAACATATCTTATTGT  
TTTTAAATAAATACTGTGTTTAAACATGCTAAAAAATAATCATTTTT  
AGAATTTCTATTAAGAAAGTTGAATCCTCAGAAAGTAAAGAAAGACTCAC  
TAATAGGTAGTTTTTGTGTTTTTTTTTTTTTTTTTTTTTGGAGACAGGATC  
TTGCTCTGTCACCCAGTCTGGTGTGCACTGATGCAATCTTGGCTCATTC  
AACCTCTGCTCTGGGTTGAAGCAATCTCCACCCCAACCTCGCAAGT  
GGCTGGACTACAGGCGCATGTCACTACACCTGGCTACTTTTTTGTATTTT  
TAGTAAAGTTGGGGTTTACCATATTGGCCAGGTTGGTCTTGAATCTG  
ACCTCCAGTGTATCCAGCACCTTGGCTTCCCAAGTGTGGGATAACAGG  
TATGAGCCACCACACCTGTCTAACAGGTAGTTTTTACAACCTGAGTTCC  
TATCAGAAGTATATTAGAATCTTTTAGCTTGACAGAATTAAGCAGAGATG  
CAGTGAATATACAAAACCTTGCTCTTTCAAAAATGAATTTGCCCTCAAACAG  
TAGTTGTTGAATGCCTATTATATCTTAAGTGCCCTCCAAAGAACCCTGAA  
AAAATACATACATAATGAACCTTATGTTAGGGTACCTCCCAACAAATCTCT  
CCTAGTACTTTGTATAGCCACACTATATGTTTTTTTAAACCACTGCCTTTG  
TAAACATCACAGTATCACTCAAGAACCTCTGTCTCATCCCTGGAGATCAG  
TGACAAGGAGATAGGTGGCAGATGATGTGAGGCCTGAGATATGCTGCCAC  
AGCTCTCAATAAACATGTAACATCTTAATAGTCATATTTGTAATAATCAGC  
CAGGACAGGGTTTTAAGGTTAGAGTCTATGTTAATAATAACAAATGTTT  
AGTCATGTGATTTAAGTTTGGATAAGAAAGGTAGGACTCGATTACAGAGA  
ATTTTGAAACTAGGGAAGGGAGTTTAGAATTCATATGGTAAGTAATTGG  
GCAAGCCACTATGAATTCCTGAGCATCTCTCATGAAAGCAATTACTCAGA  
AAGGAGAATTTACAGAGATTTATGGAATATGTTTCCAGGGTAAGATATG  
GGAATGCTAGAGTTACCACTCTATTTTTGATTTGACAAATATTGTGAAGA  
ATCACTACATAAACTTGGCGAGTATGTAAAGGATTTCTAACCAGAACCAT  
TTGGCATTTAGGGCAAAGAAATGTCTACTCTGGATGATAGCGGTGTGTGT  
GGTGTACTAGGAGTGAAACAGCGGAGTTGGAGTGGGAGGCAGAGAGAT  
GGATGGTATACCCACAATGGCTATATCTGGATTAATCTTTGAGCACCAC  
ATTTATATACACCTCGGATCTCTCCATCATTGCTTACTGAAGAGGTGGAG

FIG. 3 (35 of 52)

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GGACGTTGGCATGAAAGCTCCAAATGTGTTTTTTAGTTGCTTTCTTA  
ATATTAAAAACGAATTGATATAATCCACAAACCATAAAAATTCACCATTTT  
AGTAAGTGCACACTTCTGTGGATTTTAGTATAGCCACACTATTATACAGC  
AATCACCACCTGTCTAATCCAGAACATATTCATCACCCTAGAAAGAGAC  
TTGGGTTTACTTGTGGCAGTCCCTCCCCA

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GGTCTACATGTGCTCGCAAGATTGGATATTGAAATATCAGCAAGAAATTA  
AATGACATAGTAGTCATTATGCCTAAATTATTGTTATTTTTTATTGATTGAAA  
AAAGTTGAATATTTCAAATATCAAGGTAGTAGTGAGATATAATAAAGAGA  
GAGTCAGTTCTAAGTATAGAATTGCTGATTGAGTTAAGCTCTGTTCTCCA  
ACATTTGGGCCACATTGAAGAGACCATGTAGCTGCTTTCAGCCTCGGTTT  
CCTCCTTTGCAAAATGGGGATTACACTACCTGCCTCACAGAGATGTAAAC  
TTATGACATGTTATCATGATTGCCAGGGCCACCTGTTTTCTTTTAAACA  
TTGAAATCACTGTGCCTGAAACAGGGATTTCCCTGCCCTTTGTGCAAGCT  
CCAGAAACAGGAGTCAGCCTGAGTCCCGCAGCTAAGAACGTGGATTCTGG  
TCATTTTCTCATAGCGAACACACTTCACAGGTCTTCAAGGGAGTACATT  
TTCCTATAACTCACCTTAATCTCAGTTGAAGCCTCGTTTCTTATTTTGCA  
CTGTGGCCAAAACTAAATCTCATTTCTTTACGTAAACTTCAGCAATTC  
AATAATAGTACAGTCATTTTATGTTTCAACTGAACCAAGTCAGGGTTCCA  
CTCCTGCCTCCCTTCTGCTCTGAGGACATCCATGAAGTGGAGGGGGTC  
TATGTAGCCTGGAGCTATTGGTGAGGGGCGATGGGTCCGTGGTGGTCTTG  
GGGAACCTGCGGGGCTGTGTCTGGCTGGTCTGGTGTCTGGTGATTGGCCTT  
GTTCCACGCGGTTACGCTGCAGGACAGTTCGTGTCTTCTTGTCTTAAT  
GATCAGCTTTTAGGCTCACGGGCTGTCTCTGCTGAGATATGGAATAGGA  
CAGCCTCTGGATCTTCTTTAAACTCTCCTGGGGCCACAGGGGACTCTGTT  
TGTGTCTGTGCCACATAGGATGATTCTGCCAGACCTTTGCTGCCATTT  
CTTGCTGTTCTGCTGTTTTTAGTCTCTGGAGGGCTTGCAGTTTCTTTGGG  
GTCCCTGTGGAAGCAAAGCAAAGTCTCTCCACGCTCAGATGTCTAAACG  
TATCTGGGTTTTATCGTCCACCCATCCCAGAGCTCAGTCTAGAGGAGGGG  
GCAGCCTTCGGGTTCTCTCTCTCCCTCCAGAGCCTCTTCTTTGCACCAG  
GGCAGCCTCTTCTATCTGTTGGAAAGGGCTGTCTGGTTCTTGAATATAG  
AGTTGCAGGTTTTCAGGGGTGTAGGCTGAGGTAAGGCAAATCATCATGG  
AATAAAAATTACCTGTGTCAAGGAACAACCAGAGCTGGACAGTTTTTAA  
ATGTGAAAACCAATTTTATTTCAGGACTATGGCGAGAGGTGAAGTAAGACC  
TCAGTATAGAATGGGCTCAATTCCGAATGCAGCATGGGCAAATGGGAAT  
GTATAGCCTAGGAGCAGGGTGGGAACCTGTGGATGAAGAATTACTAAAAG  
GGCATATCAGGGGTGAGGGGGCGTCTCTGGCTACACCCACTAATACTGTT  
GCTGAAGAAAGCCTGGTGACATCACTGGGGAATGGTGGGGGATGAAGAA  
TCCAATCAGATGGATATTGAGGATAAGGGATCTTGATAAACTGGCTTAG  
GAGGGTTTTTGTCTAAACTGGTTTTTCATAGGTAAGTCCACAGACAGTCT  
TGGAGAAAGTTTCAGGGACCTACGGTTTGTTCGGGCAGATGCTTTGTCTC  
TGTACACTGGCACTGTACCTGGCTTTCTTTAGTCCCTCCCCCTTTT  
TTTTTTTCTGGAGTAGTTTTGGGAGACCAGAGGAGCAGGGAGTTAGGGAG  
AGTAGTCAGAAAAGGCCAGAGAAAATAAGGAGGTGTCTGTAGGGAAAATC  
CTTAAATCCTCTAATTAAATTAATTTAATTTATTTATCTGGGACAAGGTC  
TCACTCTGTTGCCAGGCTGAAGTGCAGTGGTGTGATCTCGGCTCACTGC  
AGCCTCGACCTCAGGGCTCAAGCAGTTTTGCCACCTCAGCCTCCTGAGTA  
GCTGGGGCTCACAGGTGTGCACTACCATGCCCGGTAATTTTTGGGTTTT  
TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTGTAGAGATGAGGTTTCGCCATG  
TTGCCCAGGCTTGGTCTCGAACTCCTAAGTGATCCATCCACGTCGACCTC  
CCAAAGTGCTGAGATTACAGGCATGAGCCACTGTGCCCGGCCTAAATTCT  
CCAATTTTTTAAATGCTTCCCTGTTCCCTGTTCCAGATTTGGGATATTGAC  
TGCTGTTAAATCAGCGATTTCTCCCTGTGGAGAGGTAGCCAATAGGAAGC  
AACAAGAGTGAGGAGTCCTTATATCGAAATAGAGGGTAAGAGAAGAGACA  
GATGTTATCTTGGCAGTGATTAAAGAACAGCGAGTCTGTAAGCAAAGCAA  
AGCAAGGCTCCAGGTGCTGAGAAACAATGGCTTTCTGGGGAAGCGTCTG  
TGTTCAAGACCTTAAGTTGGAACATCTCTGAAGATGTTTGCCATGAAGG  
TTTTCTTCTGAAGTTGAGTCTTTTCTCATCTAGGTAGGCGTGTGTTGGAGT  
CTCTATCAAACAGATCCTGTGTTTATTAGGAAGCTGTGGTTCTATAAGCC  
CCATGCTAATTTTGCAGGTAGCAGGGTGGCCCTGGCCTGACCCGGGGACA

FIG. 3 (36 of 52)

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TTCTTGTTCGGGTCA...AAGCCGTTTGCTTCTTCTGCCTTTTATAAA...  
 AGCAGAGTTCGAGCTACACAGGCTGTCTGTGTGGCTGCTATTAGTTAATC  
 AGAGAGTTTTTTTTTTCTTGCCTTGTCTTCTAATTTGTGACACATAATT  
 AGCCACAATATGTGTTTTTCAGTTGTGACACTGGCCTGGGAAACCAAGGGA  
 TGTTTAGAGTGGATTTCCTTGATTTTGCAATAATTGTGTGTTTTTCTGCA  
 TCTTCTTTAAACACAAATTCATGGAAGCAAAACATGGAAGCAAAGTACC  
 CTGGACATCCCCCTTCTTTATGAAATTGATTTCTCTTAAATGTAATGTT  
 TGCTTGTTCCTTACTTTAAAAGCAATTTAAGAGTTTATTGAGAAAGTGA  
 GCCCTGGAAACATAGATGCATAGAGAGAAAAATTCTACCACCCTCAGGTCC  
 CTATTGTCTTCTCTCATAAAGTGTAGTTTCAGGGCCTTTTAGAAGTTTCT  
 TTTCTGCTCTGATTTGCATGTTTGTGAGTGTTCCTATTTAAGTATTTGG  
 ATTTGGTCTGCAAATCCTATGAGAGATGGCAACAGAGTAGGGATCTCAA  
 GCCTGCAGGTTGTATTAAGTCCAGCAGGGCCTTGATTTACAACAGAGGG  
 TCCTTGAAGACATTCCATATATTATGCTAGGGGAGTGGCCAAGCAAACCTT  
 TAATGTGTCCCTATGGTGGGATATTTGGGGTTAATACCTGCCCTTCTCTT  
 AATTTCTTTTCTTTTCTTTTCTTTTCTTTTCTTTTCTTTTCTTTTCTTT  
 TGTAGTCTTGCTTTTGTCAACCCANGCTGGATTGGAGTGCAGTGGTATGATC  
 TCAGCTCACTGCAACCTCCACCTCCTGGGTCAAGCAATTCTCCTGCCTC  
 AGCCTCCCAAGTAGCTGGGACTATAGGCACACACCACCATGCCTGGCTAG  
 TTTTTTTTTTTTTTTTGAACNGAATCTGCTCTGTGCGCCAGGCGGGA  
 CTGCGGACTGCAGTGGCGCAATCTCGG

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CGCTGSCATCCCTCATATCCATGAGTGTCTGTGGGCGCTGCCTCTGAAA  
 TAAATCCTGCCTTTGTCTCCAGTTCACTCCAGCCACCCATCCTGGGGCT  
 GCACCCCTCCTCCTTCCAAGCCCTCTCCCTTCTCCTTCTGCTGCTGCTGT  
 CATGTCAAGCATATGCATCAGTGGCACCAGGACATTTGAAATGCAACCAG  
 TACAATTGGGCGCGGTTATGCCTACCAGTTTTCTTCTTAAACATTTTA  
 TATTTATGTTTGAAAGCATGCCACCTTTCTTCACTTGCCAACTTGACAGA  
 TTTATTAGTTGACAACATCCGCTGATAGCATCAGTAATAAGTTAATTGTT  
 TTTGCACATGTAGCTTTAATTATTCTCATTATCATTATAGGAGTTATTC  
 TTTGTAAAGGGTAAGTGGATTTTCCAAAACAAACAGAAATTTGGGGTGGG  
 CCCATGGAGCGTGACTCATGAAATCAGATTCTTAGAAGGACCTCGGCAAG  
 TCTCTGGGTTGCTGTTAATGAGCCTGGCTGGCTGCCAGGGGTGTGTCTGC  
 CCTTTATGAGGCCACCAGTGTCAAATGCTTGCCTGCAGCATTACTTGCC  
 TAGGTAGTGTCTGTTTCTACTGAACTGTGAGGGATCCAATTCTTTGTGGT  
 CTAAGTAACAATACTCAGATTCAAGGAATTGATTAATAAGCCAGAATG  
 CCAATGTATTACATTTTTGATGAAGACCATATTTACAGTGATTGTATCTG  
 CTCAGCTCAAATTAGGATTAGAGTTCTGACAAATACATATGTGAGAAGT  
 ATGAGGTTAAATACTTGAAATTTGGACTTTTCTAGAAAATCTGAATGTGA  
 TTGCCATTACATACCTTTCTGGGATGATGATTCTGTACTTTTATTTT  
 AAAAGACATAGAAAATAAATAAGAAATCAGATTGCTTGGCTGGGCACAG  
 TGGCTCATGCCTGTAATGCCAGCACTTTGGGAGGCCAAGGTGAGTGGATT  
 GCTTGAGCTCAGGAGTTTGAGATCAGCCTGGGCAACATGGTGAAATCCCA  
 TCTCTACCAAAAATACAAAAAAAAAAAAAAAAAAACAACCAAAAAGAATAAA  
 TTAGCTAGGTGTGATGGTGCCTGCTGTAGTTCCAGCTACTTGGGAGGAT  
 GAGGTGGAAGAATTGCTTGAGCCAGGAGGTGGAGGTTTCAGTGAGCTGG  
 GGTGCAACAGTGTACTCCAGCCTGGGCGATAGAGTGAGACTCCGTCTCA  
 AAAAAAAAAAATCAGATTGCTTTATTGCTGGTTTTCTTTCTAAAACCTGA  
 GATTGGTCCCATCATCCCCTGGCCCCATTGGTTAATGGTTCTCTCTTT  
 GTCTATTGAATAAAATACAGATGTCTGCTTTTGGCAACATGGTTGAATGT  
 AGACACTGCAGGCTCTTCTGACTCAAAATGAGTAAGGCTTAGATAAAAC  
 ACATTTTGAAATGCATTTCTGGATGAACAGCAAGGAAAGGAGATCTCTTA  
 AAATCCTCTTTCTGTTCCCCTCTCCCTACCCCTCCAAGTGGGCTTAAGT  
 AGGAAGGGTGGTGAGCGGCAGGTAAACACACGTCAAAGGCAGTCTTCCTC  
 TCTGAGGGAAAACACTTGTATAAGCATTGCAATCAATGGGCCTCTTTAAT  
 TATGTGCCAGTGGCAAGAGCGGTGCTGAACCCAGGGGCCTGCCTCAATC  
 CGGGGCTTTGAGGCAGAAATAAGTGGTCTCAGGTTGTTGGCATTTCCTT  
 GCCCTTCCACCCGAAGCAGACACAAATCCTCTCTGGAGGCAAGTTCCCA  
 ATTGAGCCAGTACAACCTCCACAGACTAAGATCAATCATGTACAAGCTCA  
 CAGACAAAGGTCAACCAACACACAGAGCAATAAACAAATTCATGAGTGAC

FIG. 3 (38 of 52)



CTGAATGAGAATAAACAC...AACATAACCACCAGCTGGGATGCTCTAAG.  
 CTTGAGCTGTTAGAAATTCCTGAATATAGAATAAACTGCCACAATGGCAA  
 ACATGCACTCTAGTACTTACTGTGTGCTGGGTTCTAAGAATTTTGCACATT  
 GTGCCAGATACCGACTCAGCTTCACACTCACCTCTCTACTGTGCCCTCTT  
 AATTTGCACTAGATTAAAAGGTAGAAAGGAAGAGGCAGCTATTCTGTTCT  
 TGGCTGTGCTCTGGGCAGCACATGCAAAATGGGCAGTAACAGTGGCAGTC  
 ACAGGTAAGTAGCCTTCTCACAGTGTGGAGTTAAAGGCATGGGACTGAGA  
 CGAGCAAGGTTCTTAAAGGGACAGTGGCCAGTAGATGACCAGGGGCTACT  
 GGAGTGGCTGCATGGCTCTGTGGAAGCTCAGAGGAGCCTTGGGTCTGCA  
 GGTGCACTAGCAGCTTCTGTAGTTCCTGATCTCTGGGTCCCAATCTT  
 CCCCCGTTTTTGTCTCTCCACTTCTAATTTGTAACTGACTTCCCTGTGTG  
 TACTTCTCTCTCTGATTGAAATAGCCAGACTGGTTTCTGTTTCTGATAA  
 GACATTGTCTGGTACGAACACAGTAACCTATTAAATCCGATATCTCTATG  
 AAGGAGGTACAATAATTATTCCTATTTTACAGATGAGGAAACACAGCAGA  
 GAAATAAAGTCAATTGTCTAAGGTTGCACATTTAGTCAAGGGAAGGGTTG  
 ATATAACATATAATTATTTAGAAAACATCTAAGGAAATAAAAGGCATAAT  
 TAAAAATAAACTAGGCAGGTTTAAAAAAATGAAGTAATCTATAAGTAA  
 AAAAGTATAATTGTTGAAATACATATCTTAGTGGATGGGTAAATAGCTG  
 AAGAAATGATTAATGAACTGGAAGGTAGTTCTGAGGAAATCAGAATTCAG  
 CATAGATAGAAAAATGGGAATTTACAAAAGTACACAGGAATTATAAAAG  
 AGGTTAAATATAGGGAGGGTAGAATGAGAATTAACATTGGTCTAACTGG  
 AATTTTGGGAAGAGAGATAGAGAGAATGAACAAGGCAATATTTAAAGAG  
 GTGGCTGAGAAATTTTTCAGAACCAACACAACTATGACTTTACCAGTAGA  
 GAAAACAATGTACACTGAGGAGGATAAATAAATATACTATGAACAAATTG  
 TAATAATAATACTCAACAAAGACAAAGAGAAGATGTTAAATCAGCAAAA  
 AAAGAAAGTCAGACTTAGAAAGAAATGACAATGGCAGACTACTCAACAAC  
 AACATGGAAATCCAAATTCGGTCAAACAGTATTTCTTCATGCTAGCATA  
 TAGC

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GGGAGTCCGCTATGCTCCTAAAGATTTGCACCTCTGATCTGGTTTGTAGT  
 TAGTCTCTTTTATTGCTTTATCCTACTCAACTAATTTTTTTAGTGCCTGT  
 TTTTTTTTTTTTAAATGTGTGTTGATGACTACAATTTCTAAACTCATTCTA  
 CTGATTCTATGGGTGCTTTAAATCTGAGCAGTCTTTCGCATTTACTGCCT  
 GTGATGGCCCATCCCACCAGCTAAAGTGTGTGGCCACTGCTTACAGCACC  
 ATGTGATAACGAGTAAGGGAGAGATGCCGCCAGACTCTTCTAGGAGCAG  
 CCAGTAGGACCTTCCAGGGGTTGCAAGCAAACACAGCAATATGTGGAGT  
 GTGGCAGAGGATGGCCCCAAGAGGATGTGGCAGCGGCTAGTGCAGCTCAG  
 CTTAGTCTCTAGAGGAAATGCTGGAGAGGAGAGCCAGTCTGTACAGGCAT  
 GACAGCCACAAGGACTTCAACAGCTAACATGGCTGAGTGGACTTTATGTG  
 CTATCTCAATCAGAAAAACAGGAGCAATCAGAAAGGAGTCACCTCCTATT  
 GTACCCCAAGGAATTGCTAACCTACTTGCATCTGAATGATGTCCATCACTT  
 CCCTTCATCACCTCCTCTGGGGGCTCTGCAAGGATTTGACTCCTGCATTA  
 GTGATCTGTCTCACCTACGTTGTGATTACATGAACCTACTAATGTGCTA  
 TGTGACAACCTACCATCTTAAACACAAAAACCTCTTTTGATTCTGTGGCT  
 CCCTCCAGCTACCCCTGCATTTCTCTGTCCCCCTGCCCGTCTCTGCACT  
 CACTTTTATTTTACAGCAAACTACTCAAGGGAGTCTCAGTGCTCCTTGG  
 CTCCATGTCTCCACCTTTTCACTCTCTCTCAGTTCCTCCTGTGAGGCTT  
 CCGTCTCTCAAGCTCTTCTTCACTTTTGTCTAGGGCCGCTGACATCCTCT  
 TTCTTGCCAAATTCAGTGGCCAGGTCTCTCACTTACTCAACTGCTCAGCAT  
 TGTTGGGCGCTGGTGGACCACATTCTCCTTCACCACCTTTTGCTGCTCTC  
 TCTTCTCTCCAGATGTTTCTCTCTTCTCACTGGCTACTCCTCTTTTGTCT  
 CCTTTGTAGCTCCATTTCTTCTTCTTCAACCTCACTGTGCTGGTGTGCCC  
 AGTGCTCAGTTTTTAGCTATTCTCTCTTTTCCAGTGGCATTATTAGATG  
 GTATCATGTGACCCATGGCATTATATGCCTTCTACATGACAGTTACTCCT  
 GAATATGAATCTCAGGAAAGATTTGGATTATTTTTTAATTAATTTTTTA  
 AATTTTATTTAATAAATGAGGTCTCTCTCTGTCTATCCAGGCTGGAGTGT  
 AGTATTGAGTGATGTGATTATAGCTCACTGCAGCCTTGAACCATGGGCTC  
 AAGTGATCCTCTGCTCAGCTTCTGAGTAGCTGGGACTACAGGCATGT  
 GCCACCATGCTGGATGACTTTTGTGTGTGTGTGTGTGTGTGGAGACAG  
 GGTCTTGTCTATTGCCCAGGCTGATCAAACTCTTGGCCTCAAGTGAT

FIG. 3 (39 of 52)

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CCTCTCACCTCAGCCTTCAAAGTGCTGGGATTACAGGTGTGAGACCA  
CTGGGCTAAGATTGAGATTTTGTATTCAATTGACTGTTTGACATCTTCAC  
TTGGACACCTAAGAGGTATCTCAAATATTAATTAACCTGGCCAAAATACA  
GAACCTTTTGACCCCTGCCCCCACAATACTTGGCCCTTCCCCAGACTTCTC  
CATTTCTGTAAATATCCCCAGTTACTCAACCTCAAACCTATGAATGCC  
CTTTGATTTCTTTCTTTCCCTCATCTCTACGTTGACGCCATCAGCTAGT  
TTTGTGCTTTTATGCCCAGAATATAATCTCACCACCTTCTCTCTATT  
GCCCGAGTATAAGATGTGAGTTTTTCTGCACAGTCCATTGCCCTGACCT  
CCTGAGTGGTTTGCTTCCACTTTTGACATTTGTATTCTCTTTCCCCCAG  
GGTCAATTTTTCACAGCAAGAGTGGCATTCTTTTCTTTTCTTTTCTTTT  
AGACGGAGTCTCGCTCTGTGCGCCAGGCCGGACTGCGGACTGCAGTGGCG  
CAATCTCGGCTCACTGCAAGCTCCGCCCTCCCGGGTTACGCCATTCTCT  
GCCTCAGCCTCCCGAGTAGCTGGGAATACAGGCGCCCGCCACCGCGCCCG  
GCTAATTTTGTATTTTTAGTAGAGACGGGGTTTACCTTGTAGCCAG  
GATGGTCTCGATCTCCTGACCTCATGATCCACCCGCTCGGCCCTCCAAA  
GTGCTGGGATTACAGGCGTGAGCCACCGCGCCCGGCCAAGAGTGGCATT  
TTAAACCATATATTAGATCATTGCTTTTGTGTTTGGGAACCTCCAAGGG  
CTTTGCATCATATATCAAGTTGACACCTCTCTACCCAAGCCTGGCTCTT  
TCCTGCTCTCTGTCTCTCAGCCCCCTCCACCCATTGTTGATGCTGCTTC  
AGCCACACTGGCCTTCTTGCCATGCCACATTTGTGCTAAGCCCATCCA  
ATCTCGGGGCTTTGCACTCGCATTCTCTGCTTGGCATGCTGTACCCC  
AGATCTTTCATGATTGGCAGCTTCTGTACATTACGCCACCTGCTCAAGCC  
ACCTTTTCAGAGGGCCTTCCCTGGCCACCTCACCTGAAATAGCACCTCCG  
ATTGCACCCATCCGGTTATTCTCCATCCTGTTCTCTTGGTGGTATT  
CCATCACTGATGAGGAAATGAACCATGGAATGCTAGGGCTGATGACCAGA  
ACTTTCCCCCACCCTTATTATTACAGAGGAGGAAATGAGGTGCGAGGT  
AAGATGGGCCCAGGATTTCTACTCCCGCTGGACTGCAGGCACAGCACTG  
ACCTCAGCTGTGCTCACTCTTGGCATTACCCCAACCTTCTATCTCCAAC  
TGCCCCATTTACCAGAAAGTGAATGTTCTCAGAGACGGTGAGCCACCTG  
ACTTGGACAGCAGCCCAGGGCCCCCTGGCACCTGCTTTCTCTCTCTGTC  
CATCTTTCTCTCTCAAGACCTACCTTTCCCTGTGATTCTTGCCCATG  
CTGCATTTTATGTTTATGACCTGATTTCTGAGAGGATTGAAATTTT  
ATGATTATTTATGTAAGCAAATCATTATGCTTATACAAATGAGAAAAGGA  
GTGCTTCTGGACTTCCAGGGACAAAATCTTGTCACTTGGCTTGGCTTTCA  
TATTGCTAATTAAGGACCCAGGATGTGGGTGAGATGTGCTAAAAGCTGAG  
AGGAGGCTCTGGACTCTGACTATGGGCCCCACACCTTGGGCGAGCATCAC  
ACTAGTCTTTTAGTCACTCTCAACCCAGCTTCCAGTTGAATCAGATGTT  
TGTGAATAACTCAGCAAGGCTGTATGGGAAATGAAGAATGAGGTGGGAA  
GAGGCTCTGCAAGACACACTGACTTACCCCTTACCTCTAACTAGGG  
TGTGTAGCAGCCACCCACCAAGTCTGTCTTCCAGACCAGTATGC  
TTTCTCCACCTTTGCATCTTTTATCTTCTGCCAGCCAGATGCTTGCTG  
ACTCCAGCCCCAAGCCTATAGGATAAGCTACAGCCTGCTTCTACAGACTAC  
GCATTGCAAGATCTAAGACATCAAGTCAAGTTCGGAAGCACTTGCTTCT  
CCTCTCCAGGTACACAGGCTCTCTGGAAAGCTGGTAGCAGCTGTGGAGG  
TGTGGTGTGTTACCTGCTGCAGGTGCAGAGAAGTTGACTTCACAGCCCTT  
CAGAAAGACTGCCTTCTTCCAGTTGTATTTGTGTACTTGTGTTGGTGTGG  
GGAGGATTCTCAGCTTTCTCACTCAAATTATCAGACCTTTCCATTTAG  
TGGTAGACCATTTCCCTCGTCCAGGCCAAGGGCAGATAGTACAGAGAAAT  
AGGGAGTTGTTATCCAGGGAGAGAACTTGGCTCTAAACCTGTAATAGAAA  
GGTCAGTTCTGGTCTGGAGGGTCAATTTTGATCTTTGGCTCAGATCCAGG  
AATTGGAACCAAGGCTTTTGAACATTTTAATGCAGGGGATTAAAAAATG  
ATACGAGTCAATTCAGAAATATTTGCTTAACATCTAAAGAGATCCCTCA  
AAACACTAGAAAAAATAAGAACAAAAATCTAATAAAACAAAATTTGTTAA  
ACACATTTACCAATTTTTTTTTTTTGGTAAAAATCAAATGTCATAAATA  
AAGCTAAAGTTCCTCTTGATGACTCGCTCTCTGCCCTATTCCACTCCAA  
GTAACCACTATTATCAGTCTTGCCAATACCTTCCAGACCTCTCTACCTC  
TATATACCATTAGAAGCACATGGTTTTGCAATGAGGATGTGCAGTGTGTT  
GTTTTACGTAAATGTTATCACTCTGTTCTTGTTCATAATTTGCCTTTTT  
CTCTCAATGATTGCTTGGCTATCTTTCTATTTCACTAGCATCTCTTTC  
TTTTTAACCTTACCATTTGTTTATTTAACCTTGCCTCTATCAACAGATATGT

FIG. 3 (40 of 52)

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AGGTTTCTTTCTAGTTGA. TTCATTAAGTATTTATAAACAAACGCATCAGIA  
ZATGTCCATAAATTTCTTTACGGAGATGGCAAGTAGTGGAATTGCTGAG  
CCAAAGAACATGTTTAAAAAACCCAAAAAACTAGACGCTACCAATTTTC  
TCTCCAAAATGGCCATACCCACTTACCCATACAGAGATGATTTGGAATCT  
GGCTTCTCACAAGGTGAGATGCCTTCACAGTTTCATTCTTCTGGCATG  
TCTTCCCTTTTGTATCTGAGAGAGCTGGCAGAATTGTGTCACTAAATCAA  
GGATAGAGGGTCAAATGACAGCTCAAGCTCACAGGCACCTCTGCTTTCTT  
CCCAGACCACCTGCTTTCTGCCACCAGCTCTGTTCCATCTTATAGAATG  
GTTGCCACTTGGGTGTCTGCTCCGACAGCCATGTCATCCTTTGCACTGCA  
GTTATGAAGCAGACAGAGCTAGGAGAGGGGCTTTGCCAGCCTCTGCCCTA  
GCTTGGAGAATTTCAAAGAAGGAGGGTATTGAGAGTGAGCTGCCGAAGAC  
TGGCAGCTCCCTCAACTCAACAGTTGTCTTCCACAAGAAGTCAGATACA  
TTTTTTTGGGATAAAATATTTAAAAATTATTTATTTTCTGAATAATA  
TATTTACATGATTCAAATACTGAGGCCAGGCATGGCTGCTTATG  
CCTGTAATCCTAGCAATTTAGGAGGCCGAGGCGGGAGGATCACTTCAGCC  
CAGGAGTTCAAGACCAGCCTGGGTAACATAGTGAGACCCTGTATCTACAA  
AAATTTAAAAACAAAAATTAGTTGGGCATGGTGGCTGATATGGTTTGGCT  
CTGTGACCCAACTCAAACCTCATGTTGAATTTAATCCTCAATGTTGAGG  
GAGGGTCTGGTGGGAGGTGATTGGATCATGGGGTGGGTCTCTCCCTTGC  
TGTCTCATGATGATGAGTGAGTTCTCACAAGACCTGGTTATTTGAAAGT  
GTGTAGCAGCTCCCCCTTCACTCTCTCACTCTCTGCTCCGCCATAGTAA  
GATGTGTGTGTTTCCCCCTTTCCTTCCGCCATGATTGTAAGTTTCTTGAA  
JCCCTCCAGCTATGCTTCTGTACAGCCTGTAGAAGCTGTGAATCAGTTAG  
ACCTCTTTCTTCTATAAATTACCCAGTCTCAGGTCACTCTTTATAGCAGT  
GTGAGAGTGGATGAATATAGTGCCATATGTTTGTATTCCAGCTACCCAG  
GAGGCTGAGGTAAGAGGATTGCTTGAGCCTGGGAGTTTAAGGCTGCAGTG  
AGCCATGACTGTACCACTGCTCTCCAGCCTGGGTGACAGCGAGACCTTGT  
CTCCAAAAAATAAAACCCAACTGTGTAAATGTGTTTATAAAAGTGTCT  
TTGCTCCACACCTGTCCCTATATATCTTATTCCTCAGCCTCCGACAACT  
ACTTTTATTCATTTCTTATGTATCTTCCAGAATCAAAAAAAAAAATCAAA  
TACAAGCACAGTGAATGTATTGCCCTTCTTCCCCTCCCTTTTGTTACAT  
CAGAGTTAGCATATCATAAATACGGTCTGCATTTTCTTCTTTTTCAGCTA  
TCAGCATGTTTGGAGAGGATTTTCAATTCGTGCAGACAGCATGTATTAG  
TCAGTCTTGCATTGCTATAAGGAAATACCTGAGACTGCATAATTTATAA  
AGAAAAGAGGTTTAAATTGGCTCACAGCTTCGAGGCTGTTCCACAGGAAG  
CATGGCAGCATCTGCTTCTGGGGAGGCCTTAGGAAGCTTTTACTCATGCA  
GAAGACAAAGCGGGAGTGGATGTCTTATATGGCAGGAGCAGGACTGAGAG  
AGAGAGAGAGAGAGAGAAAGGATGCCACATACTTTTAAACAACAGATCT  
TGTGGGAACCTCTGTACAGAGAACAGCACCAAGGGATAGTGCTAAACCAT  
TCATAAGAACTCCACCCCATGATCCAATCACCCACACCCAGGCCCCACC  
TCCAACATCGGGGATTACAATTTGACATGAGATTTGGGCTGGGACACAGA  
ACCAAACAATACCAGAGTGCTTTCTCATTCTTTTCTATAGCTGCCTAGTA  
TTCTATGTCTTTACTTCAATTTAGGCAGTCTCTTGTGATAGACACTTGG  
GTTACTTCCAATTTTCTTATTACAAATGATGTGCAATGAATAATTTTGA  
TCATTTTCCATTTTCAATGGGTTATGTCCATCTGTGGGATAAATCTCCAG  
GAGTGAAATTGCTGGATCAAAGGGGAAGTGCACTTGTGATTTTCTAGTT  
AGCAAATTTTGTCTATAAGGGTCATATCAATTTATAGTCCCACGCGTAA  
TATTTAACAGTGGGGATTTCCCGACAGTTTGACCAACAAGGTCTGTTGTT  
AAACTTTTGAATTTTGTCAATCTGATGGGAAAATACTAGTATCTCAAAGT  
GCTTTTAAATTTGACTTTCTTATTACAAATGTTAAGCATCATTTTACTCTGC  
CCAAGATCAAATAGTATTTTCTTTTCTGTGAACAGACTGTTAAGATCCCT  
TGCCCTCTGTTTGTGGATTTTGTCTTTTCTTTTCTTTTCTTTTCTTTTCTG  
CAGTTCTTTACATGTGAAACAAGTTATCTCTTTATCTGGGGTGTGAGTTA  
CAACTACTTTTCTCTGGCTTGTCTTGTGCTTTGACTTTGCTTCTGGTGA  
TTCCCGCAATTTCTGAAAGTGACTTTTGCATCATTCATTCTTATACACC  
CATGCTCTTGTTCACGCTGGTTCCTCTACCTGAGGGCTTTTCTTTTCTG  
CTTCTATCTGGGAACATTTTCTGAGAGAGAGTCTCACTCTCTCGCCAG  
GCTGGAGTAGTGCAATGGCGGATCTTAGCTCACTGCAACCTCCACCTCC  
TGGGTTCAAGCAATCTCTGCTCAGCCTCCCAAGTAGCTGGGATTACA  
JGAGCCCAACCAAGCCAGCTAATTTGTTGATTTATTTATTTATTTT

FIG. 3 (41 of 52)

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TGTAGAGATGGGAGTC...ACTATGTTGCCCCAGGCTGGTCTTGAACCTCC...  
 GGCTCAAGCGATCCACCCACCTCGGCCACCCAAAGTGCTGGGATTACAGG  
 CETAAGCCACCATGCCAGCCCATGTGTGGAAATCTTCTGTTTATCCCTT  
 TAGGCTTGATTCTTATGTCTGTTCTCTCCCTCCCTTCTGGATACTCTCT  
 TGTCTCTTATCTTACTCTACTTGTCTGTTACCTTGTCTGCTTATAAC  
 TAGCTCCCTCTCTATCTGAGGAGGGACTTGTGACTGTTCTCATCTCTGT  
 ACTCCAGCTCCTAGTACATAGCGCTTGGCTCAACAGATGTTTGGTGCAAT  
 GATAGATAAATCACTGGTAGCTGTTACTACCAGTCTGACTCCCTGCAGT  
 GCTTCAGCTGATCCTGTTCCAGATGTGCACTGAATATCCTTCTGTTGAAC  
 AACAGAAATAAAGGGGATGGGTGAGGAGGATAGTCTTCCGGTGGCCAAGGA  
 TATTTTAGGTACTTTGCAGCACTCAGCAATGAGGAGTGGGCTTTAGTCC  
 CCCAAGAAGCTCTCACAGCCCTGGGTGCTTTTACTGTTGAGTGTCAAATCC  
 AAGACAAGTCAATGATCAGGAAAGACCATTTTTTTTGTTCAGTGAAGTT  
 TATTTGAGAATCATTGAACAGTATGATATTTGGTAATTTTATAAATATTC  
 CCACCTTAAATGATCGGAGCAGATATATTTTCACTCGTAATTAAGGACA  
 TGATTTAAAGAGAGCACACCAGTCCAAATTGAAATGATTCCATAGCTATT  
 AAAAACTAGGGTTTTTACAGACAATGATACTTTTGGCCCCCTTTGAAT  
 AGATTAGACCAATGAATAAAACAAACAAATAAATAAATAAATAGGG  
 AAGCGGTTGCTCATCAGAATGTGGGAGCGAATGACAGAGGGTTTCTTAGA  
 ACCAAATGTGGCCGTGGTTTTCTGTGAGGCGTGCTTAAAGTGAGTAGGAGA  
 GGTGAGAGAGGCGCTGGCTCAACAAAAGGGCTGGGGATTGTCCCTGAAGAA  
 CCAGAGCTGANTTNCATCAGGAGTAACANAGGTAGATAG  
 >Cont:1341  
 CCGCGTTGAGGTTCCACGCAGTTCAAATTATGTCCAATTATCAACATTAA  
 TGCACATTTTCAATAGAACCCTGTTCCGGCTTTTCTTAGGAGGGGGGGGGG  
 GAGACGTTGTTCTCTGGGAATAAGTGTACGCAGGAGGCTGAGAAGGCTTC  
 ATTCATAGCATTCACTTACCTCCAGCTGTAGAGTGGGCTTATCATCTTT  
 CAACACGCAGGACAGGTACAGATTTTTTCTTTGAGGCCAAGGCCACAG  
 GTATTTTGTCACTTCTTCTCTCTTGTACAAAGGACATGGAGAACACC  
 ACTGAAGAAAGGGGGTCTTGTGGTTAGGGACACAGCAGTGCAGGGTTC  
 ACCCAACCCCTAGGCCCATGAGTAGGATACATGTAATTTGGTAGCCTC  
 TGTGGGAACCCACAGTGAGGTTCTTGGCCTAAGACACAGGATAACTTGA  
 CTTCTCACAGACAATAGCAGGGTCATTTTGTTGATTTAGGGTTTCCCTC  
 AAAGGCTTGGGGTTTCTCAGAGCCTCATAGCAGTAGGAACGGAGAATGA  
 AAGAGGGTCTACATTTTAAATGCTGAAGGAAGGAAGGAAGGCCATTG  
 TGTCACTGGCTGGCAATGTGCCATCCACAGGAGCGGAACAACTTGATCA  
 ATGTGGAAGGAAGGAAGAGGTGAGGCTGTACTTCTGCCAGAAATCAGG  
 CACCAGAACTGTTTCAAGAACAGAGAGTAGCCCATGGGAAGAACTGGGA  
 GAGGAGAGGCTGAGCTGGGAAAGTGGCTCCAAAGAGAGACACTCATTTTG  
 ATCTTCTCAGTCACAGCAGTGTCAATTGGAGGCCCTGGGATCACTCTTA  
 CTACCCGATTTCAAAGAAACAGGATTTTCTTGGCCTGGCTGAGAGCAAAT  
 AGCTTCCCCCTGAGTGAGGCTGTCTTCAAAGTCAGCAGCCTTAGTTGCC  
 CACACTCTGTGTCAGAGGCTTTGGCTACTGTGGCAGGATGCCAGGCAGAT  
 CACCACAGCTAATGATGGGTTTACCAGCACTTGAACTTTTGGCCGTTACA  
 GCGGAGAGATATAAGTTCTGTCTGGGCGGTAAATTTCCCTACAAGGAAC  
 CACCTGGCATTTGGGTGGGACGGATGTTGGGGCAAGGGGGGAAGACTGGGG  
 AGGGGGATGGACACATTATCGCTCCAGCACTCTTGTTCAGCCTCAACAA  
 CAGGAAGAGAGAACCCACAGGCAGTTAGGCCATGTCCATCAAATGACCCC  
 ATATTGTGGAAGAATTGACATTGCACTATGCCCAAGAGACTTGGGTGGAC  
 ATGGTCTTGGGAGTGCTTGAGCCGTCTAATTTCTCAGGGTCACACTCCTG  
 TTAACAAATGCACTGGCCAGTGCAATCAAATGTGCCATTTCTAGGACCAA  
 AGTTTGTATATCTTTTTTAATATTTTTTTTCACTTGTGTTGATCATTTG  
 CCTTAAATTAACTTTCTACTTTGTTTAAACATGGAGAATTAGCAAGCTG  
 CCAGGAGGCCAGGCAGGGAAACCAGGATGTTTCCATTTACCTTGTGTGCTC  
 CATATCTGTCTCTGGAGGTGGAGAGCTTTCACTTATATGGACCAAGACA  
 TCACCAAGCTTTTGTGCTGTGAGTCCCGGAGCGTGCACTTCACTGATCGT  
 ACAGGTGCATCGTGCACATAAGCTTCGTTATCCCATGTGTGGAAGAAGAT  
 AGGTTCTGAAATGTGGAGCACATGTTGTTTAGGTATAAAATCAGAAGGC  
 AGGCTCTGTGAGGCGAGGTGGCAAAATTTGATTTCTTGGAGGACACCTGA  
 CATATACGGTCAAAGTCTGATGACAACACCAGTAGGGATGAAGCTGGGA

FIG. 3 (42 of 52)

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GTGGGGTGGCTAAGAAL CTGGACCTGACACTATTAGACATGGGTTCC...  
CTTCAGGTCTATTACTGCTCACTGTGGCCGAGCAACAGAGCTACTTAGGT  
AAAATGGTGATGGTCATAACACTAGCCACAGGGAGGTTACGAACCTCTG  
GTGACAATGTAAGTGAAAGGCCCTTGAGAAAGAGTGAGGGAGTTGCAAAT  
GTCAGTAGCCATCAAGATCTTCTTTAAGAAATAGTTTCCACTAAAGAGATG  
ATTGCTTTGGTTTCCAGCCTTCTTTGTTTGTCTCCCCGCTGGGGCTTCT  
ACCTTTAAAGGGCTTTGGCTCTGGGGGAATTGAGTTGGCTGGGGCTTGAT  
GACTTCCAAGAGGACACAAGTGGAGATCTACTGCTGCTCTTGGCTAACT  
ACCTTCTTCAAAGATGAAGGGAAAGAAGGTGCTCAGGTCAATTCTCCTGGA  
AGGTCTGTGGGCAGGGAACCAGCATCTTCTCAGCTTGTCCATGGCCACA  
ACAACTGACGCGGCTGCTGAAGCCCTTGCTGTAGTGGTGGTGGGAGAT  
TCGTAGCTGGATGCCGCCATCCAGAGGGCAGAGGTCCAGGTCTGGAAGG  
AGCACTGCGGAGAGAGCGAGGGAGGGAGCCTGGTGAGGTGGTCTGCCAG  
GAACCATGCTTTGACATCAGAGAGTAGAAAGCTCAGAGAGGAGGAAAGGG  
CTTGAAAGAATCCCGAGCTTCTAAAGATCATCCCTCTCTGGGCCAGGCGT  
GGTGGCTCATGCTGTAAATCCAGCACTTTGGGAAGCCGAGGTGGATGAA  
TCATTTAGGTCAAGACTTCAAACCAGCCTGGCCAACTGGCGAAACCCC  
TTCTCTACTAAAAATACAAAATTAGCTGGGTGTGGTGGGGTGCACCTGT  
AATCTTAGCTATTAGGAGACTGAGGAAGGAGAATCGCTTGAACCTCAGGA  
GGTGGAGGATGCAGTAAGCCAAGATTGTACCACTGCACTCCAGCCTGGGC  
AACAGAGTGAGACTCTGTCTCATAAAACAAAACAAAACAAAACAA  
AATAAAATAAAATAAAATAAAAGATTATCCCTCTCTGAAGCTCAAGGAG  
GTTAAGGGTGTACTCAAGGGCACACAGCAGGTAGAGGCAGACTCAAGAT  
TAGAATGTGGGCTTTCTGACACCTTACAGGCTATTCTTTTAGAATAAATC  
CCATTTCTACTTTGTTTCATCTTTTGTACATGCCCCACCTACACCATAC  
ATGTATACCTTCTCTATATCTTTTGTATCCCTAATGCTGTACACTATG  
ATTTGCTTTTTCATGCAGATGACCATAACATTTTCCATTACCTATGCTC  
ACTCAGCAAGTATTCAATTTTTCTACACTGTTCTTTTTTTCTTTTTTCA  
TAACACTGTCTCATAGGCATTCTGCAAATCCTGTGAGAGTACTTTTTGTG  
AAATGTTACCACTTCTCTTATTAGAGAAGCTCCGTATTAAGGCTTCA  
CTGAGGTTGCCTTAAGGCATGATAATGTTCAAAGGCTTGAAAGACAGTT  
AAAGAGACCTGTAAAGTGCACAAAAGAAAGTTGAGCAGGAGAGAATTTCT  
GCCTGGAGCAGAGCCAAGCTGCTGGAAGAGGCAATGGGGGCAAAGGCCAG  
GCAGACAAGCCAATGGGCTCCTCCACAGCTGCAGCCAACAAGTTATGCC  
AGTCTTAAACCTTCTAAAGAAATATGTTTTAAACAAGATTGAGGACTGGA  
TTATGAGGCTAGGGGAGGCTATCACAACTGGAATAAAATAAGCCAGAG  
AAAAGTGGCTGCTTCCAACCTGCACAACTGACCTAGCTAGGCTGATGGC  
TGGGCCACCTAGGAAGGCTACTGAGCATCATATAAAACAGAAGGGACAGC  
AGGAATATAACATGGCTCTTTGTAAGGATGAGTCTGAAAAATGACCATT  
GCTGCCCCAATGCCCCCTAGCTACAACTGAAAAATTTTCAAGACTGGAGGT  
TGCAGGATGCTGGAATCTCAGAGATCATCCAGCTCAGCCCTTTATTTTTT  
AGATGAGGTCCAAAGCGGGTAAATGACTTGTCAAGGTCAAACAGCAAGT  
GAATGGTTTTCTTCAAGTCTCAATTCATCTTTTGTATATCATCTAT  
GCTCTGTGTGTATAAGCTTCACCCCAGGTAGCAAAAACTATTCTACTCA  
AAAGGGGTAGACATATGTTAGTTCTCAAGATCATCTCTTGGTTTTAGAGT  
TTAACTCAAGTGATTGGCATAGGCTGAATCCATCTCTTAAAGGATAATC  
AAATTTATGTTGAAGACTTGGTTGTCTTCTACTATGAAATGGGAAACAT  
TATCACTACTCTCCCTGTCCACCACCAAGTGTGGCCACCACCACCAACG  
TTAGTGAGTGACTGTGGTGATATGATGACCAAGTGGCCAGGTGAGCAAGT  
GGTGAGCCTGTGTCTCACTGGAAGAGGTTAAAGTCTTTCTAAAAACAAA  
TACCATGGCATCAAAGTGGCCAGAACTCCCTTCTTTGAGCTTTCCCTGT  
GTTAGAGCCCTTCTTGGGTTGGGAGTTAAACCCATAGTCTTACCTTCAT  
CTGTTTAGGGCCATCAGCTTCAAAGAACAAGTCATCCTCATTGCCACTGT  
AATAAAACAGGGACATGTCTCAATTATGTCTTCTAAACAGGTTTATTTT  
TCCTTCCCTGTGTACAAGACTTGACTGTTTATAAGAACTGCAACAGCC  
TGCCTCTCAAAGCTGCTGAAACACCTGGCAAGTTTACAGTGATATGCG  
CAGAACAGTCCAGAAGGCAGATTCTAGGCCTGGCAGGTGGGCACCCTGGG  
TGCTCCCTGTTGGATCTTGAGGCCTAACCTCTAGCCCAGCAGAGTCAGCT  
AAAACTGAGCTCTCCCTCTCCCTCCAAGCCACACTTTGCAAAGGGATTC  
CTTGTATTGTGGGCTTGAATCTTTTCTCCCATTTGCTCTGCAGGAAG

FIG. 3 (43 of 52)

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CCCTTGCACAACACA TGGATAGCCTCCAGGTCCCAAGGCTGGAGC  
CTTGTAATGGGAAAGTAGTCTTTAAATCAGATTTACTTGGCACCCTGTTT  
GCCACTGAAAGAGGCAATTTAGGGGAAAAATCTGGTCTCCAAGCACAGAT  
AACACTCTACTCTTGAAAGAGGAGACCTGCTCATGTTACTGGTCTCAGCG  
TCTCCACTGACCTGTAATAAGCCATCATTTCACTGGCGAGCTCAGGTACT  
TCTGCCATGGCTGCTTCAGACACCTGTGTAAAAAGGAGAAAAAGAGTGAC  
TTCCCATGACGGCTACGTTTATGTGTGATTCTCTCAGCATCCAGTGCA  
TGGCAGTCATGCAAAGAAATGATCTCTGAGTAAATGAATGAATGTGTGAA  
AGAGAAGTCCTTTGGGTCTAGAGAAAAGCATTGTCTAAACCAAACCCAA  
CTAGCAATGTATTGGCTAGGAGAGCTGGAGCAGAGGCTTTGACACTAACC  
TTTAGGGTGTGAGCTGTTAGATAAGCAGTATCCATTCCCAGAAATATTTCC  
CGAGTCATAAGCATTATATTACACCTGGCATTTTTGCAAAAAGCTGAGAG  
AGGGAGGCAGAGAGGGAAGGAGAGGGAGAGACAGAGAAAGAAAGAGAGAG  
AGAGAGAGAATATGCATACACACAAAGAGGCAGAGAGACAGAGAGACTCC  
CTTAGCACCTAGTTGTAAGGAAGATTAAAGTCATACTTGAGCAATGAAGA  
TTGGCTGAAGAGAATCCAGAGCAGCCTGTTGTGCCTTGTGCCTCGAAGA  
GGTTTGGTATCTGCCAGTTTCTCCCTCGCTGTTTTTATAGCTTTCAAAAG  
CAGAAGTAGGAGGCTGAGAAATTTCTCTGTTGAATACCTGATTTCACAT  
CAAGTTAAAGGAAAGGGGAAAAGAGTATTGGTGGAAGCTTCTTAGGGGAG  
GGGACTAATAAACTGAGATAATTCTCTGGTTCATGGAAGGGCAAGGAGTA  
GCAAACTATGACACATTTTGCAATGTATCACCATGCAAAATATGCATTGT  
TTTCCTGACAATCGTTGTGCAGTTGATGTCCACATTAAAATACTGGATTT  
TCCCCAGTTAGAAGAATGTTTAAATTTAGTATATGTGGGACAAAGTGGAA  
GACACACAGATTTATACATGCACATACTTTTCTTCATTCACTTCTTTGTA  
CTTAAGTTTAGGAATCTTCCCACTTACAGATGGATAAATGGGTACAATGA  
AGGGCCAATAGCCCTCCCTGTCTGTATTGAGGGTGTGGGTCTCTACCTTG  
GGTGCTGTTCTCTGCCTCGGGAGCTCTCTGTCAATTGCAGGAGCCTCTGA  
GGAGAAAATTGACCTTTCTTGGCTGGGGCAGAGAACATACGGTATGCAGG  
GTTCAGGCTCCTGACGGAGTTGGGGCAACCCTGGAGATAAGCTCACACAA  
CCCTGCAAGACCAGGTGCTGTTACCCTAGCCAATCTCATGGATGAACCAG  
ATCAATGCCAGATGAGCTCTGCCTAAATGATTTTTTGGTGAACTCTGAA  
AAGTGGAATATTGTTTCTGTAAGAATATCCATCTGAGACTCTATCTCTTG  
GTAATACCAAGAGTTATCAGTTTCTCTTTAACCGAGACACCAGCAAAGTG  
CCTGCTCCAGGGTAATGCCAGGGGAGCCCTCCATTTGTAGAATGAATGA  
GAGTCCAGGTTATGAACAGTGCCTGGAGTGTAGGAACACCCTCCTTTGCC  
TCTTTGACAGGTCTGCATCATAACACTTTTTTTTTTTTTTTGAGACAGAG  
TCTCACTCTGTGCGCCAGGCTGGAGTGCAGTGGCAGCATCTCGGCCCCCT  
GCAAGTTCCGCCTCCCGGGTTCAACCACTCTCCTGCCTCAGCCTCCCCA  
GCAGCTGGGACTACAGGCACCTGCCGCCACGCCCCGGCTAATTTTTGTAT  
TTTTAGTAGAGACAGGGTTTACCATGTTAGCCAGGATGGTCTCGATCTC  
CTGACCTTGTGATCTGCCCGCCTCGGCCTCCCAAAGTGTGTTGGGATTACAG  
GCGTGAGCCACCGTGTCCAGCCTGTAAACACTTCTTATAGCACTGAGTTGA  
AACCTTGCTCCTCCTGGTTCCTCCAGGAACTGAAATCTTTTGAGCCAA  
GTCTAGCACAGTGCCTGGCATGTACATTCAAGTGGTAGAGTTTGCTGCTT  
GAATGGGTGAATGGGAATTTGACAGCATTTTTATTCAAATTAGTATGTGC  
CAGGTATCGTGTCTGCTCTGCATTATCCAAGGGAGTGAGCCTCTGTGCAA  
GTATTTGAGACACGAGGGAAATAGGTTCTACTGTGGGAAAAAGAGCATT  
CATGGACTTGCTCTCCAAGCAGCCTTCTGATTTTAAATTTGGCTCCCAGT  
ATCTTGATATCAGGAGTCAGTCACAAGAACTCCATCTTTAGTAAGTTATA  
TTTTCCACAGGAAATCTAAAGCTGTTCAACATGTTAGTTTCTCTGTAAT  
TTGATAAGCCATAATCCATTCCCTAACACTGAGCCCTCCTGAAATTTGGTG  
TCTGGTCTGTCAGATAGCTAAAGCCCTGTCTGGGTGGCCTAGGGACTCC  
TCTGTTTTGCTCCACAGGATCCACTTTGCAAAATTAACCACTGGTTCTCC  
CGTTGTAGGAACTGCCACCTTCTCAGAGCCTGTCTTTCTTCTCTCTC  
CTTCT  
CTTCT  
TCT  
CT  
CT  
CT

FIG. 3 (44 of 52)

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TCTACCTTTTATCCCCGCTGGAGTGCAGTGGTACAATCATGCATTCA  
TGCATGATCACAGCAGCCTCAAACCCCTTCTCAGAGTCTTTATGCGGCAA  
CCAGCAGGGTCTGGAGGGTGGTGGCTCTGTGAAGTCTCCTGACAGAACA  
CAGAGATGTCTTTGGTCTGTTGATGTGATTACAAGCTGAACGAAGGAAGA  
TCAAAGCCAGTGACAGGAAGGGAGATATGCAAGGGACCCGAGCATCAGCT  
CTGAGTTAGTCCATTCTGCTTCTGGGACTTGGGATACAGGTGAGAAACCT  
TGAGCTTCTACTTCTCCATCTTCCAATTGTAGCATCCAGGACCTCAGAAT  
CTGCCAGCTAAGAGGAGCCCTAATGATTGTCTGGTGGGATATGGTGGGAC  
CACAGAGATGAAGACATGAATAGCTATTTGAATGTGAACAGCAGACGAAG  
AAATCAAGGCTAGGAGGGTGGAAAGTGACTCATCCAATAGCACAGTGTGGT  
TGAAGCAGCACTAGTATCCAGGTTGCATGAGCCCCGTGATGCTTTCGCTCG  
AGGGAAATTTGGAGCCATGGGGCAATGCCCCCTGACGTAACAGTCTCCA  
CAGTTCTGCCATGTCTCATCTGCCCCCTGTAACCTGGACCCAAATCTGCT  
ACCATCCCATCCATCTCAGGAAGTGAAACCTCTTATGTCAAATAGGTTGT  
GCAACGTATGTATCAGATCCTGTCTTCCAAGGAGACCGCTCAGGCCACA  
GCACTTCTTCCGATCCCCAATGAGCAGAAAATATCTCGCTATAAACATA  
GTTGGCACTAAGGGAGGGAGTGAAGAGTGATGATGATGTAGATGGTGTAT  
GTAGCCCCAAGGAAGTGGAAACAAGCAGAGATGGGGAGCTGGAAATGCCAG  
GATGCTCCAGCTTTTGGGAATTATTCAGCTCTTGAGTCACTAAAGCCTT  
TCTCAGCTGCAAGTTCCTCTTTACCCTGTGAGGTCATTCTTCCAAGACAG  
GAGACTGACATTTATTCAAAGCAGCAAGTGGCCTGATACCATCTTGTGTCT  
TAATCATGGGCTTCGCAGCCAGTTATCAAGGTTGATCTCATCTCATTGGT  
CTTCAATCATTTTGAACAAGAAGACAAGCAAAATAATCATGGGTTAGTTC  
TTATATTATTGTGTGTACATGCAGTGATGTCTGTTCTTGTAGTGAGCTG  
TTCTTCTCTGTTTACCCTCTTGTCTTAGAACAGAACTAAGCAATCTGCCC  
CCAACATTTTCCCCAATTTCCCATCTCATTCTTGGCACTGGCTTCTTAAT  
ATTTGTTCTTATGAGTCATTTTCTTGTATCATTTCCATGAGTCCCTCTGG  
GATCTTAAAGTATGAAAAATGTTGTGTGTACCCACACCTGTCTTGTGGA  
TATTTCTCTCCTTTCCCTTCTGCTTCTGGGATTATTTGGGAATGGGCACT  
ATGATTTTTATCATATCGCTTCCACTTCTTTATGGCATCATCTCCAATG  
GGCTTCTTCTCCCTCTTGGATCCAGGTTCTCAGATTGGGGACATGCAGAG  
TCCAAGGAACATTCCATTCTCCTCCCTGGTCTAGAACAAGGAGGGCTTAG  
ATATATGAGCAGGTGGCTGGGGCTGGCGAGCTATGTAGTCTCCAATGGCT  
TTTCCCTGATGTGCGAGTTGTTATGTGAGTCTGGGAGACCAATAAGACC  
TTGTCTCTCTTGGATCCATCAGAAAAAGCCCCCTGGGTGGGTAAAGATGG  
ATGGCAGGGCTCTCCTACTCTATGTCTTTTCTCACACCTAGTGGGTATAA  
GAGAGGGGACCACAAACAGAGGGGGCTCTGGTACCATTATCCAGGGTCT  
GGAAACATTTTCTGTAAAGGGCCAGATAATAAATGTTTCAAGGTACAATA  
CTCAACCTTGCATCTTTCAGAAAAGCAGTCAGATAATACATAAATGAAT  
GGGTGTGGCTGGACTTGTCTGCGGTCCCCTGTCTTATATCATTGTATTA  
TATCATTTTTTCTTACATACAAATTTAGAAGCAATACTTAAAAAAAAAAAA  
GCCGTCTTTTATTGAGCACCTACTAAGTGCCAGGTACCTTTTTTCCCTC  
ATTATCTTATTAATCTTTCATAATAACCTTTAAAGTAGATAAATTTGAAC  
CATTTGACCTATGCAGAACTGAGGTTGAGACAATAAATTTTAAAGACC  
GCACAAACAGTAAATGCTGGAACACGACTCAAATATGGGTAACTGAAC  
CAAAACCAGATCTTTATTTCTCACTTTAATTGTTACATATGTTTATTGC  
CTCATCTCCTGTCCACATGGTGCCCATCGGCAGACTCCTTTCTCATTCTC  
AGTGATTGAGTGACATTCTAAACTACATTGGCCTGGCAGATTACCTCTG  
TCCCCATAAATGTTTCCACATTGTCTTTTAGGATTGAGATCCTCTCTGTT  
CCCTTGTCTTCCCTCCTTTCTTCTTGGCGGTGACGTGCTGTGTGAATT  
TGTTTCTTTCTCCTCTCAGGGTAGTACTGGGACTTTCCAATCAGGGTTT  
TTAGTGATCTCTCTTCCCTTTTCTGAGTTTCTTCTTATTCCCATCACT  
TTCTCATCTATAAGTGGCAGCTTTGTTGCTGGAGGATTTCTTTGTCTCT  
TTATTCTCTTTAAGACTTTGTCACTAAGTGTCAAAGCAATCCCTTGAAG  
GTATCTGTCTTGGAAATTGTGTGCTTATGATGCTGAAAAATACTCTCTTC  
CTAAAGCTATTATAAATGCT

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GGCTAGCTGCAACTCTTGAATACAAACACATTTCAGACATGCACACACTTT  
CTGGCTCCCCAAAAGAAAAAATCAATTTATAATAATTCTGATCCT  
TTGCTTATTTCCACAACTCCATGAAAATTGTACATTGTCCAAGCAACAT

FIG. 3 (45 of 52)

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TTCTTAATATTCTCTT...TCTCTCATATCCATTTTCCTTACTGCTGTC...  
CACCTATCTCTTCCAAACTCCCTGTTAAATCCCTGCCCCAGCGAACTTT  
TATTCAATTTTGTGGAATGGAGGCTGCACTGATTTAAATTAATAAAAAA  
AAAAATCCCTACTCCATGTCCCAGATCCCTAGTTGTTTTTGTGTTTTTG  
TTTTCTGAGACAGGGTCTTGTGTCTTCCATGCTGGAGTGCAGTGGCATG  
ATCATGGCTCACTGCAGCCTCAACCTCCTGGGCTCAAGTAATTCTCTTGC  
CTCAGCCTCCCCAGTAGCTGGGAGTTCAGGTATGTGCTACCATGCCTAGC  
TAATTTTTCTTTTTATTTTGTAGAGACACGGTCTTGCCAGGTTGCCAG  
GCTGGTCTAGAACCCTGGGCGGACGTGATCCGCCTGCCTCGGCCTCCCA  
AAGTGCTGGGATTACAGGCGTGAGCCACTGCTCCCGGCTTGGGTGCAAA  
TTTGAGCTTTCTCACTTATTAGTGTAAAGACATACAGCTAATTTCTAAATC  
TTCCAAACCTCAGATTTTTTCATCCATGAAGTGAGGATTATTATAGAGCTC  
ACTAATAACATGGCTTCAAAAAATATATAATGCCAAATTGAGATCAAAAT  
AATAAATCTATATTACATGGGAGATCTTAATGTACCTCTTATATTATTGA  
TAGACTAAGATGATCAAAAAATAGAAAGAGAGCAGTAAGGAGAGCAAGC  
ATTTAATCAATAGGACCAATACATTTTATCAATAGGATCCTCAGGAATA  
TATACAGAATACCAAACCTAACAACTGCAGAAAACATGCCAAACATTTAG  
GTACAGACATTGTTGGAAAATGCAATCTTGAAACGAGTGGACTGACATTC  
AGAAGATATTAATAAGAGCACTAATGATGGGGATTGCAACCATGTCTTTA  
CTGACTTCCAGAAGCTTCTTACAGTAAACATGAAATCACATAATTTCTTC  
CACTTTCTACTGTTTCTTGTCTGGGCTCTGTCTGCTTACTGTCTAAT  
ATCTTGGCCCCCTTAAAGTTGCTAATCTTCCAAACCTCATTCTGTGACT  
GGGCGCTGGTCTTGTTCATGGGCTTGAAATACTGACTGTACACTTA  
TCTGGAGCATCCAGTGCCTACCACCTGACCCAGATTCTCATTGCGCTCC  
TCCCTCTCCACCTATTGGAATTTGCTCATACCCGTGTGAGACCCCTCC  
TTTCCCCCATCTGAATTTTTATCAAGACAACGCACTGCCATACTCCCTC  
GTACCCTGCTCTGGGCATCAGACTGAATGTTTGTTCATTGAGGATCTG  
CAGCTGCATCAGTTTCCCCAGCACCGTCCAAACCTTGAGCATGGCTAGT  
CCTAAAGCAGAGAATTAGCCTTTCTATCCCTGCTGCTATACATGCTGGGA  
CAAATAATAAGAAATGACAGCATTTATGATAATGCAGGCTGCAGGAGGC  
AGGAGGCAGGAATCAAATTCGTGCTTATCAAATAGTGCTCCAATCTTTG  
AATATTGGACTATAGAATATGTCTATGGATCTATGCTCAGGTGGGTTCCCT  
ATTACTCACTCCACTGAGGCCAGGTTGTGGGATTAGCTGTCCAAGAGGGA  
GTTTCAGTCTCACAGCATAGGGTCATTCTGAGAATTACTGGCCCACTT  
GTGTGGAGACCTCCAGAGAACAGAACTCTGGGTTGGTGCCATGTACTTCCA  
GGAGGAGAGAAGTGGCAGGATGCCAGCCCCACAATCAGAGGGGAAGGGG  
CAGAGCCACATGTATGAAGATCCTCTCCCCAGTACGTGCCAATCACAGGG  
CTTCTAGCTTTTGGGCCAAGGAAACAATGTGGGAAGCAAAAAAGGACAA  
TTTTCTCTCTCTTTCATGAAGACTGAGCAGTTTTACCAGATTCCCAGG  
GAAACACCTTCCACTCTGGGTTGAATGTGAGTGAGAGACATTCACTGG  
AACACTAGAAAACTATTTCTGAGCCACTCACCTTTAGCCCTAGAAAGT  
GTTGGATTTGTCTTCTATCTTTGCCACAGTAGAGACTGCTGATAGCATCA  
GAACCTGGGCTCTGGAATTAGACAGATATGGGTACAAATCTGAGCTCTCT  
CACTTATTAGTGTGGGATGTAGAGCACTTTTAAATCCTTCCAAACCTC  
AGACTTCTCATGCATGATGTGAGGATTGTAATAGGGCCACCTAATAGGG  
GTTTTTGAGAATTAATAAAGTTATTCAATGACAGCATTTAGCAAGATGC  
CTGACCATTGAGAAAATAACAAATGTTTATTATTATTGTTATTATTAAA  
CATCTTCTGCACTTCTGACTGGGGCATCGTATCATCAGAAATACTT  
AGGATGGGATGGATTCTGCTATGGGCTGAGTCAAGGGTGCAATAATGGAG  
GAGTGAAGAAGGAAGAAATGGAGGCAGAAATCCCCAGGAGCCAGCATGG  
TACAAGGCTGAGCTAGTGTGCTGAGAGCCTCCTTGAACAGCCACAGAGCT  
TGATCTGGCCCTGGGAGGAACCTCTTCTAGCTGGCAGGACCAGCCACAA  
CAGTGGCCAGGGGATTTCCAGGGCGTGGGCTCCTAGGAGTTTCAATTTGA  
CCAAGCCTGCTGGAGAGGGGTTATAACAGGGATCCTTCCCTACTGGCAG  
GTGATTTACCCCTCGGTGAGAAGCTCAGGCATTTGTTGATGGAAGGTGG  
AAGGCCCTGTGCTGGGCCAGTGAATATCAGGGATGGGCGGGTGGCTGGAA  
AATAGCAATAAGACAATATGATAACACAGTTAACCACCACACTATGTGA  
AGCTACAATATGGGTATCTGTAATAGACAATTCCAATGTAGAGAATAATT  
CTAAGGTGTCTTCTCCCGCCAATGCCATAAGCACACGGCCTCTGCCTG  
GGTTCTCACTGTGGAATGTCTCTCTGGTCTCTCATGCCAGAGAGTGG

FIG. 3 (46 of 52)

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GAAGTACTCTCTACTTT. .CACCGGCTTTCTGTCTCTCTCTGCAGCC...  
CCTCAGCCCCCTCTGCACAGGGAGGTTTCTCTCTCTGCTGCTGCAGTGCTT  
TGTACTTGTAGTGGTACCTGCACACAGGTATTGGTGTCTTGTCTCACC  
ACCCTACATCACTGTAAGCTCCCCAGGAGCAGGCTTCTGTTTGACTCAC  
CTGTGATCCTCCACCTCCACCCCTGTAGTGCCTCAAGCATTGAGGACAAT  
CACTGGCTGCCCCCTTAACCCAGAAATGCTGCCGAGACAGGAGGCCATGGC  
CCAAGTTCCTGGAATGGGGTATTACTATGTCTCAGCACAAAGGCCTTTGCAC  
AAATGAAGGCTTTAAAAATGCAGTCTTAGTCAGGTGGAGGAGGGCTTATA  
GGATTCCCAGGAATCTGGATCATTCTCTTGGAGAGCTTTCCCTTGTCTCTG  
TTAAAACTCACATCCTACGGCCCCAAATAACAACAAAAAATGGATGTAAAT  
TCTTGAAATAACTTGTGGATGGGGGAACAAGGCCACCCCCCAGATCTGC  
CAGAAGCTTCAGGTGAGGGTCCCAAATGCCAAAAAGTCTGGTATCAGAGA  
GGATGGCCAGTGACCTGGGGACACATGCCCTTGTGTGTCACTCAAGGA  
GCAGCAGCCTCGGCCCCGCACAGTGACCAGGACCCTGGCTTCCCACGCTG  
GGCAGGCTCGGTGTCTGATGAAGGGAAATGCCCTGGCAGCACGTGCTGTCT  
GTCTCTCGTGTCACTTACCTGGCTTGTCTGCGAAGAGGCCACTCGCAT  
TTCTCAATTTTTTATATTTTTTTAATTTTTTAAATTTTTTATTTATTTT  
TATTTTATTTTATTTTATTTTATTTTAAATTTTTTTTAAATTTTAAATTA  
TGCTTTAAGTTTTAGGGTACATGTGCACATTGTGCAGGTAGTTACATAC  
GCATACATGCCCATGTCTGGTGCCTGCACCCACTAACTCGTCTCTAGC  
ATTAGGTATATCTCCAGTGCTATCCCTCCCCCTCCCCCACCACAA  
CAGTCCCCAGAATGTGATGTTCCCTTCTGTGTCCATGTGATCTCATTG  
AATTTCTTTAAAGGTGGAATCTCTCAGTGGGGTCTAATCTGTTTCAAGAA  
ATCAAAAGAGTATCCTTGGGAATGACTGGAATCCAGAGTCTCTGGTAA  
TCCTCATAAACAACCTCCTGGATGTCTCTCAGCACATCTCCACCTTGAA  
CGCAGGAGGCTGGTTCAAATGGAGGAGCATCGCTCTACTGCATTTTTTT  
TTTTTTTGGCCTAAAGTGCAAAAGGGGATACGTTTCTGTAAATAAATCA  
ACTGCAAAATCGCTAGTTATGCTGAGCCCTGTCCCGTGTGTGGACACAAA  
GGAACCAAAGGCTTTTCTCCCCGCCCAACACACACATAACACACACACAA  
AATCATAAAAACATACATACCCCCAACACATAACACACACACACACAC  
ACAAAAATATATACACACACACACCAAAACATGCCACAAACCTGTGTCT  
CAGAGATAGATCCTACTGGTGGGTTTGTGGTCTCGCTGACTTCAAGAATG  
AAGCCGTGGACCTTCGCAGTGAGTGTTACAGCTCTTAAAGATGGCATGGA  
TCCAAAGAGTGAGCAGTAGCAACGTTTACTGTGAAGAGCAAAAGGACAAA  
GCTTCCACAACCCAGAAGGGGACCCAGCAGGGTTGCTGGTTGGGGTGGC  
CAGCTTTTACTTCTTTTGGCCCCCTCCCATGTTCTGTTTCCATCCTATCA  
GAGTGGCCTTTTTCAATCCTCCCTGTGATTGGCTACTTTTAGAATCCTG  
CTGATTGGTGCATTTTACAGAGTGCTGATTGGTGGCTTTTACAATCCCT  
TGTAAGACAGAAAAGTTCTGATTGGTGTGTTTTACAATCCTCTGTGAAG  
ACAGAAAAGTTCCCAAGTCCCCACTGGACCCAGGAAGTCCACGTGGCCT  
CACCTTTCAACTCCATAATGGCATGAAAATACATATGTTGTACAAAACAT  
ACATACACAAAGTATACATGCATCTCCCCAAATATACACATACCACAGAA  
ACATACACACAGGAACCTCAGCTACCTGTCAAAAGTCTGCATGGTATTGC  
CTCTGCAGTGAGTAGTTAGAAAAGTGAATTTGTTTTTCAATAAATTGGAG  
TCCTTAAAAATCGTTGTAAGATAGAAAATTTTTTAAAGTATATAAAATAA  
AATATGTATGTCTTTGGTCTAGCATTACACATGTAGGAATTTATCCTA  
GTGGAGTAATCAATGATATATGCAAAGATTTGACAAGCATATTAAGCAC  
AGAAATTATGTATGCATATGTGTGTGTATATATATATATCTCATACATA  
TAATAATGTAAAAGTGAAAAATACTCAGATGTTCAAAATTGAGGATTAGT  
TAGACTATGATCTGTCCATATGTGACATACAAGTTAGCTGCCCTTATTC  
TCTCGAGCTTCAACCTCCTATAAACAGTGTCCCTGTATATCAGTATTGG  
TACAGATAATCGAACTTATTGAGGTTTTACATGGGGCAATAAAGGCAAGA  
GTTTATGAATACTCCATACTACACTAGGTAGCACCCCTATTAAAGACAA  
ACTCTTCTCTCTCATTTCCTTCCCTTCCGGAACCACTTGGTTGAATCTC  
TACAAGTCTCTATTGCAACTGCCTCAACATGGCACCCCTCCCTGCATCTCC  
ATCTTCCCTGTCTGAGAGCAATGGCCTGCTGCCCCCACTCACATCCT  
CATTTCATTCCAGAAGTGAGCAACACAGAAGTGCTACAGTTACCCCAACC  
ACCTTCTTAGAAGATAAGTTAGTGTGTGTGTGACTTTTTTAAATTTTTTA  
CTTCTCTTTCTTCACAATCTCATCCCATCCCAAGAGGTTTATCAAGA  
AGTTCTCTAAAGATATGTGTCTCTTATGGAATTTAACAGAAATCAGGGA

FIG. 3 (47 of 52)

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...GAAATCAGCCATCAGGGAATAACATTTTTCCAGGTCTTTAGAC  
ATAATGGAATACCTTGCAGTAATTAGATACACTATTGTAGAAAAGTATTG  
ATGAAATGGAACGATGTTTGAGATATCATATTGAGTAGAAAAGGCAAGAT  
ACATTAAGTAGGAAATGTATCTTACAAAATAATTTGTGAGACACACTCCT  
ATATTTGTATGTTATATATAAATGCGTATGTGAAGAAAGGCTAGAGGATGAG  
ACCACAGTCTTCGGTGAAGTTTAAGAGATGATGCTGCAGCATGCTCAGAA  
AGGCTTGGTATAGTTTTTTCCAGTAATTAAGGACTGATCTTAGGTAAAT  
GTCCATCCTCTCTAACTGCACCACCTTTTGTCTGTAAAACAGGAAGGAT  
GGTATTTACCCCCAGGGTCATCAAAGGATTTGGTTGGAGAAAAATAAATA  
AATGGGCTGAGCCAGACCTGGCACAGTGAGAGCACAGTGGTTGACTATT  
GTGCTGGCCTGTTGTTCTGTGTTATTGACATGCTGCTGGTGGTGGTCCA  
GAAGCTATTACCTTAATTGGTTATGTGGATTTCCCTCATACTGAGCAGC  
TGTGTGTGGTGTGTGTAAGCATAGCCATACACAGTAAGTACAAGGGCAA  
ATGTGATGGAATAATGCAAGGAAGTGCAGATAAATAGCTAATGGGCTGTA  
GAAGGAAGCTAGTCTTGGAGGGCTTGATCAAGGAAGGTCTTTTGCATG  
TCACCTTTGAAGAAGAGGGGACATAGAAGAGGTATAGTGCATCCCGGAGT  
GTACCTGGGAAGGGAACATGAAAAGAGGACATTTTTCTCTGGGACATGGGG  
ACTCCACTTGCATGAACCTCTGGAATTGGGGCAAAGAACCATCATGAGAAC  
AAGGGCTTCTTGAACCTCCAGGCTCATTTGGCTGATCTAAACCCTGTGT  
CCCCCTTTCTTCACTCTCCTCTGTTTTCTATACCTGTATTATTGGACT  
GGACTGGAAGCCACCTGATCTATCACAAGTACCTTGAAATGTGTTGAATA  
GGTGTGGCACAGTCTTAGCAGAGTGGCACTACCCCCACAGGAATTTGTT  
TATACCTTTGGCATGGAAAAATAGCAGGAAATGAGTGATCACTGATAACTG  
AGGATGCTATTATTATTGGCCAAAGGAATACTTGTGTTGATTTGCATA  
ACCACTCACAAACTGTTGATTACAAATGAGTACCAGACCTAGCTCCTTCA  
AGTAAAGGATCTTGAGAACTGAAGGCAAACAGAGCTCCAGGAGTCCAAGA  
CAGAGCCACAGACCACGAGGATCCCTGGCCAGGTAGGTGGTCTCTCTGC  
ACTGGCTTTCAAGGCCAACAGGATGGATGGGGAAGTAGAGTAGCATCTGG  
CCATCTAGACCCTTGCTTTTTATCCCCACTGGAAGCACATCTGAATTTCT  
AAATATGATCTCTGAGACCTGCCAGAACACCTTGCTCTCAGCCCCAGTA  
GCAGCCTGCTCTCTCCAGGAGGCTTCCACTAACAAAGTAGGGCATTGCT  
GGAGGGCCAGGCAGACACTAGCTTAGGAAATCCACCAACCCTGGAATGC  
TAGTCCCTTCTCTGAAGGCTCAGAAGACTGACTTTAGAGTCTAGAAAATA  
TTGGTCCTTGGGAACAGATTTTGAGTGCAAAGAGATGGACTTCAGATGGC  
CAGATGCACTGCTTCTTAGGGAATCTGTGAAAGCTCCCTGCATTTATC  
TTAATACAGGCAGCAGATTTATGAGTACCCCCGAGGGATGGCCCCAGGT  
CCTCCAGCCTGTGAGCATCCTTCTGTCTTCCAGCAGCACCACAGTATCTT  
TATATGCTTTGGATACCTACGTTTCTGCCAGACATCTCTGCTCTGATG  
TTCTGGCTGCCAAATTCTCTGTCAAGCGCTCCAATTTTGTGTCTCTT  
GATTTACCCCCAATGACAAAGGCAGTTGTGCTTCATGTATTTCAGGGATA  
CTGCCAAACCACAAACAGGTTAAAATCAAATAGCAGATATCCCTGTTCT  
AAAGACCCATCAGCTCTACCCACCTGCTCCTGCTCACCGTCTTATTGTT  
GAGTCTGAAGCCCTTCTGTGCTATTTTATTTTTTGATGAACAATTTA  
GTTCCCTTTGTCTCACTCCTAAACCTTTCTCAAAGGATTGGATTTGTACA  
CAAACCTGCCTATCTCTGCAATCTTAGAAGTGATATGATTCTGAACAAATC  
ACTTAACTTTTGATTTTTTATTGGTAAGATGGGAATACCAATTTTGTCTC  
CACTTCTGTCTATGTTGGCCTGGGCTGATGTTGAAAGCTCTCGGTCAAC  
TGAGATAGGGTGTGCAGAAATTTATATATATAAATATATCTCCTCCAACCC  
CTCCCAATGAAGCAAGTCACGTGAGTCAATCCTACCTAAGATATTAGGG  
ATTGAGCCTCCTGGGACATTTGGTGGCTTAGGTTTTCATGAAAAGAGGTT  
GCAGAGCAACTGCTTTTTGTTAGGCAAAGATTAGGCTACTGCAGAGACTC  
AGCAAACCTTCTATAGAAGGTGTGAGATGGTAAGTATTTTAGGCTTTGCTT  
GCCAGATGATCTCTCAACTAGTTAACCATGCTATTGTAGCCTCGAAGCAG  
CCAGAGACGATCTGTAAACAAGAGCATGTAGTGTGGCATAAATATAGTA  
CCGCG

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GCAATAAGTCTATTTACTGTAAAGTTAATCAAATTTACATTTCAGAACAC  
TTAATCTGCAAGAGTCTTTTCCAAGACCCTATACCTAATTTGTGTTTAC  
AATTTTATATTTGTTTTCTTAAAGAAGACCACCAATATAAACTATATCCA  
GCCTTCATGATAAGTACATAAGAACTATGCAAATAAGGGGGAAAAA

CAAAGAAAAATACCTAC TACTAATGGTTCACCTTCTGAATAGCACAT....  
TCATAATGATACAAGCACTCATTACTAGTCTAGGAAAATGAAGATATAAT  
TGCATTAGGAAGATCAAGAGGTAGGAAATGTGGATGTGTGGTATAGAC  
TAGGGCAGGACAAAGAACCTAAATCCTCATTCTTCTAAAGATAATTGTAA  
TACGTAAAACTCAAAATTCAAGAAGTAACAGTAAAAGCGGTCAATTAAGAA  
ACAAGCACTAAACACCAGATAGGAAGCGAGAGATGGGGGAAGAGGGCAAG  
AATCTGATTATTTTTCGAACAAATTTTGTAAAAACCATTTGACTGTTTAC  
ATGTAGAACTTGGATCTTTTTTAAAAAACACAAAAATAATACTATTAT  
TTTTTAACCTGGATTTTTTGAAGAAAGATAAAAGTCTCATTCTAGTAATT  
AAAACCTCATTCCAGGTTAGTCCACTCAAACTTATATTCGAAAATTAAAA  
CTTTGGGAGGCTGAGGCAGGCAGATCACCTGAGGTTGGGAGTTTCGAGACC  
AGCCTGACCAACACGGAGAAACCCCGTCTCTACTAAAAATACAAAATTAG  
CTGGGCGTTGTGCATGCCCTGTAATCCCAGCTACTCGGGAGGCTGAGGCAG  
GAGAAATTGCTTGAACCCGGGAGGCAGAGGTTGCAGTGAGCCGAGATCACA  
CCATTGCACTCCAGCCTGGGCAACAAGAGTGAAACTCCATCTCAAAAAAA  
AAAAAATTTAAACCTCTGGAAGTTGAGTTTGCAGATATTTCAT  
TATGCTCATTAAAACTTGTATGTTTGGAAAATGTATGATGAGAATTGA  
GGTTGGGGGATGAGAAAAAAGAAAAACATCAACCCACAGCCCATTCAA  
TTTTCAGCCCCGACCCACAGCTCCGGGAAGGGCAGCAGGTCCATCCTTCA  
CTCTTTCTTCACCTCTTTCCCTCTCTGCTCTTCCACCTCTAAGTTG  
GAGCCCAAGAAGAGGCACTGGGAAATGGAAGTCTTTGTACGTGGTAC  
TTGCCGGGAAGCTGCCATGAAGACCTGGCCCCACGGTGGGGAGGGAATG  
CCCAGCTGAGGCCTCGTGCCCATGCTAGGATAGACTCGTCCAGACATGTC  
AGGTGGTCTGACAGGGCAAGCAGCAGGAAGTCATGTATGAGTATGAAGT  
ATCTGTATGCAAGGGCGGGGAGAACACGCGGAGGAATGGGCGTGAGAAA  
ACAGCACAGTACGTTCTTTAGCAGCTGTCTCTGCTCAGCCATGGGAGTC  
ACCAGAGAAAGAGGCTTGGAGGCGTTATTTTCACTGTGAGATGTGAGTGT  
AAAAAAGTGCCCAAGACACAGTGAGTACCAGGGAGATGCCCTCTTCCCT  
ACCCGAATGCAGAATGGCCACAGGCCTTAAACACACACATGGTTCTCTCA  
GAGGAGAGAGGCCTCCACAGTGGACACCCGCATTCTCCCTGGTCAGCAG  
CAGCAGGGCGAGTGCTGGGCCATCATGAAGCTTCACAGGCAATGAGCTCT  
CAGCAATAACAGGAACAGTGCCCTGGGGGACTGTAGCTGCAAGACCGATT  
TCATGTAAGATGGCCTCTGAGGACTCCGAGATACACAGGCTGAGACTAG  
CTGGCAGCTCCAAGTTCTTGGTCAGAAGAGAACAGGAAGTAGGGAAATTG  
GAATTACTGTTACTACAATTCCTTTACATCCGCACAACCATGAGGTCCAG  
AGAGTCTCTCTTATTTTTTTTTTAAAGACAGGGTCTCACTCTGTGCCCCA  
GCCTAGAGTGCACTGGTGTGATCATGGTTCAGTACAGTCTTCACCTCCCA  
GGCTCAAGTGACCCCTCTGCCTCAGCCTCTCAAGTGGCTGGGACAGCAGT  
TGCATGCTTACCAGGCCTGGCTTTTTTTTTTTTTTTTTTTTTTTTTTTT  
TCGGTAGAGACTGGGTCTCTGTATTGCCAGGCTAGTCTCGAACTCCT  
GGGCTCAAGTGATCCTCTGGCCTCAGCCTCCCAAAGTGTTGGAATTACAG  
GCATGAGACACTGCACCCAGCCAGTATAGTCTTTTAACAGCTTTATTGAG  
GTACGGCTAACATTGAAAAAACTACACAAATGTAAAGTATGCAATTTGAT  
AATTTTGACAAATGTACACACCAGTGAAACTATCACTACAGTCAAAATAA  
TGAACATATCCATCACTCCCAATTTCTCAGCCCCCTTGGTAACCCCTCT  
CTCCCAACTCCCTGCCCCCTAACATCAGACAATACTGATGCATTCTGTC  
TCCATAGGCTCATTACATTTTCTAGAATTTTACATAAATAAAATGACAG  
AGTATATACTCCTTCATGTATGGCTTCTTTCAGCCCAATTATGTCAAGAT  
TCATGCTTATGGCTGTGCGTATCCTTAGCCCATCTCTTTGTCTTGCTGAG  
TAGGATACCATTTGCATAGACAGACCAGCTTGCTCATCCATTCACTCTT  
GACAACGTTGAATTGTCTCTGTTTTTGAATGACAAATAAGGTTGCTAT  
GTACATTCTGTATAGACATTTGTAAAGCACAGCATTTTCACTTCTCTTG  
GGTAAAGACCTAAAAGTGGAAGGCTGAGTCATATGGTAAATATATATGT  
CTAACTTTTTAAGAAACTGTCAAACTGTTACCCAAAGGGATTGTACAATT  
TTACATCCCCACCAGCAGTGATGAAAATCCCGTACTTCCACATCCTCA  
CCAATATATGGTGTGGTCAATCTTTTTAATTTGGACATGNTAATGAGTG  
CAAAATGAGGCCCAGAGTGCTGAAGTTACATTTGTATCCTTTTTGGCAT  
CCAAAACAGGTGTCAAGCATAGAAAAACACTTGTTCCTTGAATGGTCAG  
TCATTTACAAGTGGAATTCATTACAAACCGGTAGTTCTACTGGGTTAAAC  
TATGCCTTACTGTCAACAGGCACATACACATACAGACAGACAGGAAGGCA

FIG. 3 (49 of 52)

CAGAGACAAGGCAGAGC...TGATAAGAAGGTGACCTGGGCTCTAGCTCT...  
GCCTATCACCTAGTAAATATTAGTTAAGTAGCCATGAGTAACTCACTTA  
ACTTACCACAGGCTCCATTTTCTTATCTGTAAATAGGAACATTGAAACA  
GCTAATCCCCAAGGTTTGTGGATAATCAGAATTACAAAGATCAATGACAT  
TTCTATGAGAGAAACATATTTCCAAGTATTTGATGGAGTACATCAGACAC  
AAAGGAAAGGAAACTGAATATTTTGGAGTTTATTTTACCAAGAAA  
TTCACATTTTGTAAATTTTCAAGAACTACCTCCTGAGGAAAGTGTAGCTG  
CACCCATTTAGAAATGATAGAAAACATCAATCTGTCTGATTCCAAAGCCAA  
GTTCTTGCTACAACGAGAAATGAAACAACCTGGATCCCTACAGATGCAGAG  
ACCTGGGCCCCACAAATGTGAATTTCTGTTCCCTACCGAATAGAGTTACA  
BTTCATAATAACAGTACTCCCTCACTTTTCCACAGTCTCACATTCCACAG  
TTTCAGTTACCCACAGTCAACTGCAATCCAAAAATATTAATGAAAAATTC  
CAAAAAATAACAATTCAGAAGTTTTAAATTTGTGCTCCATTCTGAGTAGCG  
TGATAAAATCTTGTGCCACCATCCACCTGTCCAGCTTATCGTTAGTCAT  
TGACATCGTCTGCTCCTGACATCCAACCATGACATCATCATGACTCTAT  
GATCCAGGATCACCGAAGCAGATGACCCTCCTTCTGACATATCATCAGGC  
CAATATCAGCCTAAACACTGCATCACTATGCCACATCAGTCACTCACT  
TCATCTCATCAAGGAGGCAATGGATCACCTCACATCATCACAGAAGAAG  
AGTGGGTATAGAACAATAAGATAATTTTGGGGCAGGCATGGTGGCTCAGC  
CTTGTAAATCCCAATACTTTGGGAGGCCAAGGCAGGAGGATCCCTTGGGCC  
CAGGCATTCAAAACCAGCCTGGGAAACATAGTGAGACCTCCTCTCTCTGC  
AAAAAAAATAAAACAAATTTATCCAGATACAGTGGTGCATGCCTGTGGTC  
CCAGCTACTCAGGAGGCTAAAGTGGGAGGATCACTTGGTCCCAGGAGGTC  
GAGGCAGCAGCTAAGCTGTGATCGTGCCACTGCACTCCAGCCTGGGCAATA  
AAGTGAGACCTGTCTCAAAAAAAGGTAATTTTGAAGAGAGACCAC  
ATTACATACAACTTTTATTATAGTATATTGTAGAATTGTTCTATTTCATT  
ACTTATTGTTGTTAATTTCTTTCTTTCCTTAATTTTCTTTTCTTTG  
AGTCGGAGTTTCACTCTTGTGCCCAGGCTGTAGTGCAATGAGACGATCT  
CAGCTCACCGCAAATCCCGCCTCCCGGTTCAAGTGATTCTCCTGCCTCA  
GCCTCCCGAGTAGCTGGGATTACAGGCGCCTGCCACCATGCCAGCTAAT  
TTTGTATTTTATAGTAGGCGGGGTTTCTCCATGTTGGTCAGGCTGGTCT  
CGAACTCCTGACCTCAGGTGAGGCCTCAGCCTCCTAAAGTGCTGGGATTA  
CAGGCTTGAGCCACTGCGCCTGGCCTCTTTCCTAATTTATAAATTAAAC  
ATTGTACAGGCATGTATTAATTTATAGGAAAATCATAGACATATAGAGT  
TGGGTACTATCCACAGTTTCAAGGCATTCACTGAGGGGCTTGGAAACAGCC  
CTCCTCAGATGAGGGGGGACTACTGTCTCTCTCAATCATTTCTTGATTC  
AATCCTCAACACAAATGTTTGGCCAGGTCTTGCTCTGGAGACAAATTT  
GCTAAGGATTTAGAGGGGAAAAAATGTAGTTCACTGGGAAAGTCACTCT  
GCTCCACTGACAGCAACTTAAACCCAGGCCATGACAAGTAGAAAGGCC  
ACCCCTCACTCTCCTTCAACCTGGAGTATTCAGGAGTCAATCATATTTCA  
GGACCACCAGGAGCAAACTGGGAAAAAAGTGAAGTGCCTTGAGGAAAGCAA  
TCAGCTCCACAAGGGGCTTAAGAAACAAGCTCTGGGAGGAGTGGTTGGAG  
AAGAGTTGGGGACACATCAGAAATGCCATCAAATTTCTAAGGGCTACCTC  
GTGGTGTGACACCTGTGTCATCTTCAAGGACATAAACAGATGGGATAAGCA  
GATGAGATTACAGAGGACATCAAAATATTGGCTCCCCAGAAGGGAGAAC  
ATTCTAGTAACAGAGCTGCCAGCTGCAGAGTGGACTGTTTCAAAAGCA  
ACAGGTGCCCTGCCTCTTGAATCACCATCTTCAAGGAATGCAGTAGAAG  
GGACTTAACTCCTGCCCTGAAGAAAAGGTTAGGCTAGGGAAACAGCTCCA  
AAATTTTAAAGGAAGCAACATAGGCATCTACTGGGAGTTTCTAAAG  
CCTTTGTTTAAAGAACTAAAGAGCTGGGACAGGAAATGCCAAATTAAT  
TAATAGAGCCTTGCTTTAAGACAATGCAAGTGGATGGTAATGAAGGAATG  
AGTCTTAGGCCTTGATCAACCGTATTAAGCAATGCTGAGCATGGAGCCA  
ATTCTGTTCACTAGATTTGCTCAGAAAGGGCCAGACGAGAAGGATTTTTC  
TAAAGGCACCTACTACAAAAAGCTGCCAAGGCGTCCAATGGAGCCCAGA  
GAGAAATATGCTAACAAATAAAAGTTGAACACCCTCAATAAAAAAGGGTAA  
AAGTAATTAATAGAAAACTACTGAAAGCTTTTTGAAACCAAAAGTAGTC  
AGCATTGGTAAAAGTCTACAAAAGTGGACACTTTTATATAATGTTGGCAG  
GAGGGTAAAAAGACATAACCTTTTGGAGGACAATTTGGCAACAGAGTAC  
CAAAAACCTTACAATTGAAGAGAACTTTGGCCTGAGTGCAGTGGCTCACA  
CCTGTAATGCCAACACTTTGGAAGGCCAAGGTGGGAGGATTGCTTGAGCC

FIG. 3 (50 of 52)

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CAAAAGTTTSGAGACCAGCTGGGGTAACACAGTAAGACCTCGTCTCTATG  
AAAAATAAGAAAAGTTAGCTGGGCATGGTGGCATGTGCCTGTGGTCCCAA  
CTACTTGAGAGACTGAGGCAGGAGGATCGCTTGAGCCTCGGAGGTCAAGG  
CTGCTGTGAGCCATGTTCTGCGACTGTTCTCCAGTCTGGGTGACAGAAT  
GAGACCCTGTCTCACCAGAAAAACAAGGCAAGAGAGAGAGAGAGAGAGAA  
GGAGAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGATGGAAGGAAGGAAA  
GAGAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAA  
AAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGGAGAGAAAAGGA  
AGGAAGGAAAAGAAAAGAAAAGCAAGCAAGCAGGAAAAGGAAGGAAGGAA  
GGAAGGAAGGAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAA  
GAAAGAAAAGAAAAGAGAAAAGAAAAGAAAAGAAAAGGAGAGGAAAAGGAAA  
AGAAAAGGACAAAGAAAAGACCTTTGAACCTGAAATTTCACTTTTAGAGA  
TTCATCTTAAGGAAATTCATTCCAATAGAAATTTATCCCAGGATTATCT  
AAATATTTGCTTTTATTTCTCTAGTAATTTTATGGTTTAACTTTCTCA  
TGTTTAAACCTTTAATTTATTTGGAAATTTATTTTGGTATGAGAAAGTGTG  
ACCTTTTGTGTTTACTTTAAAAAAATGTATTACGATTATTTTATTTAG  
AGACAGGGTCTTGCTCTGTCAACCAGGCTAGAGTGCAGTGGTGTGATCAT  
AGCTCACTGCAGCCTTGAACCTCTGGCCTCAAGCAATTTCTCCCTCTTCAA  
CTTAGGAGTAGCTGGGACCACAGGCATGTACCACCATGCCCCAATAATTT  
TTTTATTTTTTGTAGAGACAGAGTCTTGCTTGTGCCCAGTCTTGCAAT  
GTTGTCTCAAACCTCTGGGCTCAAGTGTGAGCCACTGCGCCAGCTGCCTTTTTATTT  
AGCACTGGGATTACACGTGTGAGCCACTGCGCCAGCTGCCTTTTTATTT  
TTTAATTTTTCAGATGCTTTGTTGGTTCCAAAATAGCACTTATTAACCCA  
CGCTTTCCCTCTGGTTTTAAATACTGCAAGTTTGGCTTTGAAATACAA  
CCCCTGCTTATTCAAGGCTACATTCAGGAAATCTGAGACCAAGAGTCT  
GAAGGCCAGTTTCTTCTCAAACCCAGGAGGTGGTAAATGTGTCACTT  
CCACACTTTCTATCTATTTCTAAGAACTCTTCTTTCCAAACTCTGACAT  
GCCCCCTGGCTCAGGTCTATAGAAATTTCCAGGGTCCACAGACAAAGCAGA  
ACTCACTTATGGGGAATCTGGGAAATACTTATCTGTTAAACCTGCCCCA  
TATGGTGACTIONAGATTGTCTAAAGCCCAAAGCATCATTTTCCACCCCAA  
CCATTTCTCTCTCCAGACTTCTCTATTTCTGTGGTCCAGAGTCAAGATCT  
TGATATTACCCTAGAGTCCCCCTTCTGCTCTCTGCATACCAGATGCCC  
CTCCCTCCCAGATCCATTCTCCACCCTCCCTCCCATCAGTTTGGTGGG  
CCCATCACCGCTTCCCCGGCCAGGCTCTCCTTTTGTGCGCTTGGAGCA  
GCAGACTGATCTCCAGCCTTCACTCACTTCTATGTGGTAATCTGTTGTGT  
TCATCACTGTGAGAATCTTCTGCATCCCCTCACTACTCTGCTGAAAACAC  
TCTAGTGGTCTCTCATTTGCTCATTAAATGAAAGTCTAGATATTAAACGTAG  
AAGGCCAGCACAATTTGCCCCATGCCACCTACCTCTCTAATCTTTTTCT  
CCTTACTCTGACAGACTCTCCGTCTGTCAATTTATGTATCTTTTATTGCT  
CTCTTCTACTTTTAGTATGAACTGGATTTATGGATTTTTTAAACATTGCT  
TTCAAGTATGGAATAAAGAATTTTATTTATTTATTTATTTATTTTGA  
GACTGGGTCTCACTCTGTTGCCAGGCCAGAATGCAATGGTGCAGTCATA  
TCTCACTGTAACCTCGAATTCCTAGGCTCAAGCCATCCTCCTGCCTCAGC  
CTCCTAAGTAGCTATGACTACGGGTGTGCATCACCACATCTGGCTAATGG  
AATAAAATATTACAATGCCTAATCTTAATTTTCAAAATTTTAAATTACAT  
TGTACCTAATGCCCATGCATTTACTTTTTTCACTGGGTCAATAGCCCTCA  
CTTTGGCAAAGTCCCAGGCCCAAGGTAAGGCCTTACTTTTTCCAAACTC  
ATCTTTTGAAAGACATAAGTGCTGTAAAGTTGTACCACATTAGGTTCTAG  
GAATTTTTCATCAAAGACTTTATCAGACTATTTTCTCTAAGTTGAGAAA  
GAGCTGGGGGCAGAATATGGCACTGAATGACTGAAGAGAAGGCACTGAAA  
TCAGGCCAGAGGTTGCTGGAAAGAGCAATGAGGAACACCAGCAGCAATGA  
GGAGCCSGTGATGATTTTGGCTTACAGGGAGGTGTGTACCACACCGATT  
TTATCTCTACGTGGATGAACCACAGCTGTGCGCTCCCTTGTCTCCAGGAC  
ATCACACTCTCCACATTTCCCTCCCATCTTCCGGCTTCTGCTTCCCGGGC  
CCTCATCTGCCCCATCTGGGTGAACACTGGTGGTCAACTGCTGGGCGT  
ACCTTCCCGCTCTGCACACCCTCCCTGGCCACCCACCCACTCTCACGGC  
TCGCACTGCAGAGGAGCCGATCTCTAGCTCCAGCCCATCTGCCTCTTCT  
GAGCTCTAATTCATGTAGGCGACTCCTGCCGGTGTGCTTCCAGGCCC  
ATCATACTTCAAAGCATTTTCCCTCAGAACACCATGTCTGGCTGCTCC  
CTCCAGAAGATACATCTCTCAAGCACATCCCCGGGCTCTCACCTGGATG

FIG. 3 (51 of 52)

ACTGCATTACCTTCTC ACATTTGCCCTCCTTTGGATGTATATAGA.  
GTTTTAAATAACAAATCTGATGTGCTTGCTCTCCTGCTTGAAACACCTCA  
AAACTGCCCTTCAGGATAAACCACTGCCCTTGACATGTTTACAGGTTGCC  
ATGGCCTGGCCCTGCCATCTCTTCAGCCTCATCTCATGCCCTTGCCCC  
TCGCTCTCTGGGCTTCTGCCTCCCTAGCCCTCCTTTAGGTTCTCTAACAC  
ACCATAGTCCTTCTAGTGTGGGGCCTCTGCAAGTGCTGTTCCCATTGCC  
TGAGACATGAATCCCTCTCCCTATCTCTACCTGCACCTTCATCTGATTAA  
TOCTACCCCTTCCTAGTCATGATGTTGCTTTCTCAGGGACTCTCTCTGAC  
TTTTTAACTAATCAGGGTCTCCCCAGTATATATCTTCATAGCACTCTGT  
ATTACTCCTTCTTAATGACCACCTGCTGTAGACTGAATGTTTGTCTTCC  
TCCAAAATTCATATGTTAAACCTAGCCCCAAATGTGATAATATTTGGAG  
GAAGGCTCTTTGGGAGGCAGAGCCCTCATGAATGGGATTAGTAGCCTTAT  
AAAAGAGACCCCTGAGGGCTCCCTTGTCCCTCCACCGTGTAAGGATGCA  
ACAAGAAAGTATGGTCTATGATCCAAAAGCAGACCTTGCCAGGTACCC  
AATATGCTGGCACTTGAACCTCCAGCCTCCAGAAGTGTGAGAAATAAAT  
TTCTATTTTTTCATAAGCCACCGAGTCTATGGTATTTTGTATAGGAGCAC  
AAACAGACTGATGTGCCACCCAACCATGATTATACGTGTAATTTATGGTT  
TCTCTGCTAGTAGGGATGCACCATGGGGTTAGGAACACGCTTTTCTTAT  
TTCCACACAGTCTTAGCTCTAAGCATGTTCTGAATCAAAGATCCCCA  
TCTTTTATGAATGAAGGAGTCACTGAATGAATTAATGAAAGAACTGATAA  
CCCTCAATAATTATTCAGCCTTTTATACCTACTATTAACAAGCTTGCAAT  
TCTACTCCAAATTTATTTGGGCTTTAACTCTATTTTGGCCAGCCACATTT  
GACATTCCTGAAGTAAATCTATGCTTTCCATCCTAAGTCAAGGAAGGAC  
CTGGACTAGTAGGGCCAAGAAAGGTCTAAATTCATGGGTGGGAGAGAGA  
GACTAAATCTGAAAGGAAGAATAGATTGAGCAAAGGTGTAGAGATTGGGG  
AAGGCTGGACATTTGGAGAGAAGGAAAGGAAAGTGAACCTAAACCAAAC  
AGTCTCACAAACACAATCTCATCTTCCAAAAGTCTGTGAAGTAAGAAAT  
ACTATCCCAGGGCCAGGCAGTGGCCCATGCCTGTAATCCCAGCACTTT  
GGGAGGCCAAGGTGGGTGGATCACCTGAAGTCAGGAGTTCAAGACCAACC  
TGATCAACATGGTGAAACCCCATCTCTACTAAAAAATACAAAATTAGCTGG  
GCATGGTGGTGACACCTGTAATCCCAGCTACTTGGGAGGCTGAGGCAGG  
AGAATCATTTGAACCTGGGAGGTGGAGGTTGCAGTGAGCAGAGATCGTGC  
CACTGCACTCCAGCCTGGGTGACAGGGAGACTCCGCTCTCAAAAAAAAAA  
AACAAAAAAAAAACCAAAAAAAAAACAAAAACAAGAAATTACTATCCCAG  
TTTTGCAGATGAGGCAATGGAAAGCTCTAAAAAGTTAAGTAGGAGAAACAA  
ACATGAAATGTATGTCTTATGCTTTTCTCATCTATTTCTCAGCCTGG  
AATGTCCATTCTCCCTCCACTATGCAATCTAACTCTTCAAGCTAACACA  
TAGCAATGTCTGAGAAACCGTCCCTGTGTTCACTCTGTTAGCCTCACTTG  
CTCCCTCCCATCCCTCTGTTTCTTTCTGTTATAACACTTCTCTATTCT  
GCTGGCATCACAGTCATCTCCACCTGCCTTCTCACAAGTTAAAAAGCTTG  
TTAAGGGCAAGTGGTGTCTTTGCCACCTCATTTCCAGGGCTTCTAACA  
CAGTGCCTCATGCATGACAGAGTTGTAAAAACAGGTTACCAAGCTGGCTTC  
AGGCAGGTTTGCATGGAAGTGTGCTTTACAGGAATACCTGCTCCCCCAG  
GCCCTGGGTCTTCTCTGAGTCCAGGCTCAGACTCTCTCATCTGCTCG  
TTCTCTCTTGGGGAGCCACAGTAACTTTGAGCAACTTTGCATGGGATAGA  
ATGGCCTATTAGGGGCAGCAAAAGACCCCATGGAGGGAAGAGTACAGAA  
AGGGAAAACGATAATCATATTTTTTAAGATGTGCATTTTCTTAACAAAA  
TGCTCTAGTACTTGTCCAGACTTTCAAAGTCAAAAACCTAAGCGTCTTT  
TCTTGAAGATCATCAAAGGCCCCAGTGGTCTTTCAGGTATGTCAAGCTTT  
CTAGAAAATAAAGGTAAGTCATAATCACTTAACACACATGGCTAAATGGC  
CATTTCTTCTAATTTATCAGCACTGTTACATATTTCTATACTAGAAAA  
AATTTATATTTATACTCAGGGTGGTAAGTTAAATTTGCCATCGAAGTAAA  
GCAGAAAGAGCGTAGCATGTATGTATGTAACTCAACTGTGCATGAGAC  
AAAGATGTCTTGAGGAGAATGAGTCTAAGATGCGCTGAGCAATAGTACC  
C

FIG. 3 (52 of 52)

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## &gt;Contig1

GCACCCATGTTTCTAAAGGGCATACAGCCATAATAACAGGATGGGTGAG  
GATATAGACAGCAGATGACAGAGAGGAGAGTGAAAGCTGGGAATCCCAGC  
TAAAGGCATCAGGTTTATGGAATGAGTAGGGGACAATACTGTGTGTGTTT  
ATACACACATGTATATGTGTGTATATGTATACATGTTTATGTATATATAT  
AATTATATGGTACCATTCTAATTGACAAAATAATCTATCACATTTTACA  
TTATCAGATTTTACATCTATTGTTCTAAATACACTCAGTCATCAGCCCTG  
TGTGTGGGCTCTTACCCATCCCATGCACACCTCAGCTCAACCACTGATG  
GATGGATCATCTGCCTATCAGAGGTGGCATATTGAGGTGAATCCATGGCC  
ACAGCTGCAGCACTTCTACCCACGCAGAAAGGCTCCACAAGAGGAGGCA  
CACCCGCTCTGACTGTCCCTAAGCTCCTGACATCTTACCCCATGAACT  
GCTGCTCCTGGGTGCTTCTGCTTGGCCTGCCACCCCTTGTAAGTGTCT  
CACCATTGACACAGCTGGTGCCCGATGCAC

## &gt;Contig2

NAAAACGAATCGTCACTATTGAAGCCTGTCTCTCANC GGATCGTGACTAA  
GAACCCCTCCTTGCTTCAAGTTGCTGCTTTCTAGGCAGAGCCACCC  
TACATCTTAAATATATTGATTGATGACTTACGTCTCCCTAAATATATAA  
AACCAAGCTGTGCTCTTACCAACTTGGGCACATGTGGTCAAGACCTCCTG  
ATGCTCTGTGTCATGAGTGGGTGGGTGTTCTCAACCTTGAAAAATAAAT  
TTCTAAATTAACGTGAGACCTGGGTGAGATTTTGGGGTTCACAGCAACAA  
TTTAAAAAACTCACCATTGACCTGAAATTTTACCTTATGCTGTTGCTCA  
CACTCCTCCATGAAAATAGACGCCATCCTATGAGTTCCTCAGCCATGTC  
ATGCCACACTTCCAACATGTGTCCCATCCACCATCTGTCTTCTATTGC  
TGCATCCTACCCAGGCCCTGATCTCTGGACCCATTGTTGTATAATTAAGA  
ATTTGGGGCTGGGCATCGTGGCTGTGGCTCACTCCTGTGATCTCAACATT  
TTGGGAAGGTGTATTAGTCAGGATTCTCCGAAGGATGCAACCCTAGGGA  
TCCTCTCTATGACCCTATGTCTA

## &gt;Contig3

CGCGCTCAACCGACCGATTTGCGCGAACCTGCCCATGCCCGAGGACAGTG  
TAATCCTAAAACGTCCCCTGAATCATAAGGATATGAGTGCGAAAGTACGG  
TTCCCTCTGTACCACTTTCTAACAACGCTATGTCCGATCCGTGCACTAA  
CCCCGCCCAAGTCACTGAAACACTGATGGGCGCTTCTCTACAGGTATCC  
AGGGCCAATACCACTACTCCCTCCTCCTGTCCCTTCCACTCTCTAG  
AGGCCGCGGATGCCATCCTCTATTAGCACAACCGAAAACGACGGTGAAAG  
TACCACGAAGCTCACGATCTGATCGGTGCGCCAATGCGGTTACAACGGCT  
GTCATCCCAACCCCGTCCCATCCTCCATATTGCCCCCCTATGAGGAT  
GGCCCTATCATCATGACCTCCAAAATTCTGTCTCTCCCGACGTAATGCC  
GCCCTCGAACCGCTGACACCATCAAGTCNGTCACCTCCCAAATACTCC  
TCCTAATCACCGGCCGAGTATCCCCGGTTCCACAATACCTCCTTGAGAC  
GGGCCGATATCACACAC

## &gt;Contig4

NGGAGTTTAGGTCAACTAGTAACAAGTGGGATTTGCGACTCAGGTCTATC  
TAATCCTCAAACCCACGTCTTGACCCCTACACAGACTGCCCTCCCTCAG  
TCCTCTGTGTGGCCTCAAGAAGGGTCTGGACATTCAAGTTTAAAAATCCA  
TCCAAAGAATCTATGGACCCAGTGGTCTCTGGAGTCAATGTTCTGAGGCT  
CAGAAGGGCCAGGCAGGAGGGAGCCGCTCTACACAGTCTGAGCAGAGT  
GGGCTGTGTCCCGGCACAGCAGGGGAGATCATAAACAGAATTCTGCCCTG  
GGCCCTATTTAAGTAGGACCTTTAGGCTGCCGTTGTCATGACCACAGGTC  
CCANGTCTGCACGATTGGCTGTGTGTGGAAAATCTTCACTCCTTGCGGCC  
TTGTCTTTGGCAGAGAGCACCGCTGCTTCTCTGATGGCCACCAGGGGGA  
GGCGCTCCCTCGGAACGGTTTGAANGGGAGCCTCACCCACACGTCCT  
TCCGTGGTACCCAGCACAGCTGCTACCCATGGTTACCCACAGGCCCAGC  
TCTGCTCTGAAGAAGGAGGAGTGGTGGCGATCANGCCTTGTCTGCATCCC  
GTGGCTGCCCTTTCTTTTCTTT

## &gt;Contig5

GGGAGCTAACCGCTCACTGGGATTACAGGTACGCACCACCACGCCTGGCT  
AATTTTGTATTTTATAGTAGAGACGGGGTTTCTCCGTGTTGGTAAGGCTGG  
TCTCGAACTCCCAACCTCAGTTGATCTGCCCGCTCAGCCTCCCAAAGTG  
CTGGGATAACAGGTGTGAGCTACCATGCCTGGGCTTATATGTTTCTAGTC  
CAAACATTTAGCTACCTTTTTTTTTTTTTTTTGGAGACGAAGTCTCACTCTGT

FIG. 4 (1 of 61)

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TGCCAAGCTGGAGCACAGTGGCACAATCGTGGCTCGCTGCAGCCTCAAC  
CTCCTCAGGCTCAGGTGATTCTCCACCTCGGCCTCCCTAGTAGCTGGGA  
CTACAGGTACGCACCACTACACCTGCTAATTTTTTTGTTTTGTATTTT  
TTGTACAGATGGGGTTCTTCATGTTACCCANGCTGGTCTTGAACCTCTG  
GGCTCAAGCAATCTGCCTACTTCAGCCTCCCAAAGTGCTAGGATTACAAG  
CATAAGCCACCATAACCGGCCTACCTACTTTAACTTGTGGAATTTTCTA  
TAAGGTCANGGATGCCTGNGGGAACAAAAGTTTCTCCCTTGGTATATGCA  
AGTAAAATCCACATGCTGCCTCCC

&gt;Contig6

AGGACTGTAGCTGTTGTCTAGTCACCAGGCTGGACTGCTTGGCATGATCT  
CAGCTCACTACAACCTCCACCTCCTGGGTTCAAGGGATTCTCCTGCTTCA  
GCCTTCCAAGTAGCTGGGATTACAGGCATGCACTACCATGCCCGGCTAAT  
TTTGTATTCTTAGTAGAGACGGGGTTTCGCCATGTTGGCCAGGCTGCTCT  
CAAACCTCCTGCCCTCAAGTGATCTGCCTGCCTCGGCCTCCCAAAGTGCTG  
GGATTACAGGCGTGAGCCCCCGGCCACATGTAAAAGTTTATATCTCTGT  
TGTTTACCTTGTTTTTGACCTAGTCTTTCAGTGATTTGAATCTTGATTCT  
AGTCTTTTGTATTTTAGTGGTACTTCCAGCTTGTGTCTATCTGTGGAT  
GACATATGAGTCTTGCTTCTTCATGCCAATTTAAGAAGACTGAACGGGAA  
TAGGTCAAAGGCATGGCCATGAGCGATTCTCTCCAGCTTTTCATGGTGT  
TCAGCTTCAAATCTATTACATATTGGACCTGCAAGCCATCATCTTATCC  
ACAGGCTATCATCATAGGTGAATGTAAATTGGGTTTAGGTGGCCAAGCTG  
AACGTGAGATATNTTC

&gt;Contig7

AGCATGTTCTCTAAAGGCCTATCAAAGCTGACATCAAAGGGATAAGTTCC  
AGTTACCCAGCTGAAGGGAAGGAGGGTGTTCAGATAGAGGAAGGATAAG  
CATGACCTATTCAAGGCCAGTGAAAGAAGCGTGCAACGGCCAAGTCAGGA  
GAACCTGAAATTGTGTCAAAGAGCTTGGATGCAAAGAGCCGTGGGAGACT  
ATTGGGGGTTTTAAGCAGGGATATAATATTCAATTCAGCATGCAGTAAAA  
GGTCACTGGCACCTGCCATGGGCCAGGACTCGGGCTCTACATGATTGCGT  
CTGTTTTGGAAATATCACCTTGGCTGTGAGATGAAGAACAGGTAGGAGGG  
TCACAAAACCTGAAGCAGAGAGACTGTTGAGGAAGTAAGCTGTTTTTGTG  
TGGACTGTGGCAATCACAGAGGCAGAGGATATAAATGCACAGAGACACAA  
GGCATGTGGGAGGCAGAAGGAATCAAATACAATGAGTGATCAGATGTGGG  
GTTAGAATGGTGAGTGANAAAGACATACTCAAGGTGACACGCCAGGTAT  
CTGGGTGGATGGTAAGACATTATGGACTAGAATCGAAGAGGAGGTGGGG  
ATGGACATTCTTCCGTTTAGAGGGGTTCAACAGGAGGATTTGCCGGAAC  
ATGGAGAGGATTAACCAGGAATCCGGTGCCTTTTTCCAAACTGGGTTGGA  
GGGG

&gt;Contig8

GGTGAATGCTTTGGCACGCTGTGTAGATTTTAGGTGACGGGTGGTGACAA  
TGAGTCCGTGTGAGCGCTGATTTTTTCGGCCTTTAGAGCGAGATTTATA  
CAATAGAAATTTGGCATGAGATTGGATTGCTTTTAGTCAGCCTCTTATAGC  
CTAAAGTCTTTGAGTGACTAGATGACATATCATGTAAGTTGCTGATAGGT  
TTCCAGTTTTCCGCTCCTAGGTCTGCATATTGTACTTTTCTCTTACTCG  
ACTTAACCAGTACCAACCCAGCTTCTCAACGGATTTATACCATGGCACTT  
TAAAGCCAGCATCACTGACAATGAGCGGTGTGGTGTACTCGGTAGAATG  
CTCGCAAGGTCCGCTAAAATTGGTTCATGAGCTTTCTTTGAACATTGCTCT  
GAAAACGGGAACGCTTTCTATAAAGAGTAACAGAACGACCGTGTAGTGC  
GAATGAAGCTCGCCATACCATAAGTCGTTTTTGTCTCCGAATATCAGACC  
AGTCAACAAGTGTCAATGGGCTCGTATTGCCCGAACAGATTAAGCTAGCA  
TGCCAACGGGATAAACGAGTCGCTCTTGGTGGAGGG

&gt;Contig9

GGGGTGGGGCGCCTGGTGTCTTAAAGAGGATCTCCTGCCAGAAATGGTG  
TGCTGACACTGTTGTCTCCTTGGTGTGGAACCTTGGTGGGAAGAAAGGT  
TGGAAAGGGAAATTTTGATCCTTGGATTTAACCCGAGTTTGTACTGATG  
CTCACAAGACTAGGGGAAGGATAAAGGCAGGTGAGTCACTCTAGGATGGC  
TCANTGAGCTCCACAGAGCTGGAACCAAGGCACAGGAGGGATTGAGAG  
CAGGCCTCAGTGACGTCAGCTGAGTGAACCAATGAGCAGGTGATGGGTC  
CAGGCAGAGCCCTGTCTCTTTAGGCAAAAACCTTGAAACACCGTTCCC  
ATCCTAGCCTGTGTTCCACCCAAAGCTGGCCAGTCTCCAGGCCCTGCCTG

FIG. 4 (2 of 61)

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AGCCCCAAGGAAGTGGTATGGTGAAACAGAAGGGCCATTCTGTCCAATG  
TGTGAGGAACCTTCATTTTCAGACTTGTGGGAAGCCCTGATGTTCAAAAACC  
TCAATGATATCATTCATTTTCCCCATCCATTCAATGCCCATCCAATGCCC  
ATCCGTTCAATGCCCCCTTCCATTCTCTTTCAGGGAAATGAAAATTGTTCA  
GAAATCCTTTCTCTTTTCGAGAAACCAACCAAAACCAAAACCGCGAAATTCA  
CTAAACTAGCCCAAGACACAATCCTGGGTTATTTTCTTTTCCCAAACCTC  
CTGTGTTTAAATTAATTCTACCCTGGTTCTCGGCCCTTACTGCGAAGGTG  
AACTCACCTAACCTCTCCCAAACAGAGAAGAACTTCTCTTGATAAAATG  
GGTTTTAACACTTCTAAAAACCCCC  
>Contig10  
GCTATGGTTCTAAAGGTAATGGACTATGGCGTACACAACGTCTCGCTCAT  
CGTCTGCCAGGAGGCTAAGGTATCCACGGACAATCGCTGAGCAACAGTGT  
CGTTGATCCATCTCTGTACGCACTTGTCAACATGGCAGGAGTACGGGAGC  
TGCGAGAATCCTCTCTGTGATGTCCACGGAGCATGCCGTGAGACAACG  
CCACGAACGGCCCTCGGAGANANCTACTCTGCAATGAAGACGTACGATAC  
ACACGTAGGAGTCTTAGCTCACCAGCCGTATCTAGGTATACTGTACTCGC  
GGATACTCACTCGTGCATGCGGCAATAGATCGATACGCAGTCTGCACGCC  
CATGCTCTCAGTGTGTGACCTTCTGGCGGTAGCGTNGTGGGCGCTATTAC  
TGTGCGCAGCAGGCGCNTCGTACATGTGTGGGTAGCGATGCCAGGAGCT  
GTAACATAGCAAGTCGCCCCCTACTCCTATCACTATCCCTACGCTGGAC  
CGCACTCGAGATCTGAACGCACGTCTTAACCTGCCAGTACTCGTGAGACC  
TATACTGCGCAAGCCTTGGCTAGGAGATCCTGCAGCGCCGGCAAAGAATC  
AGCTATGATCCCCCTTGGCATTATCGCACACGCACCATAGAGTATGTGCAT  
ATTAACCTCTGAATGTGCTGCAAGCAGACGGTTGCTCAACATATATATGG  
ATGTGGGGAAATCGCCCTGGTCACCGCCACTTGGCGTCAGGAGGCACCG  
CACGTCTGAGTGTACGCACGTTACTC  
>Contig11  
GGCCGAATGGTGAATTCATCCGTCTCTCGAGGGGGTGAAGACGGGGAG  
TTATGCTGTAATGGCACCGCTCACCCTGGGCTTATGAGCAGACCTAACC  
TCCCANAGTGCTGGGATTACAGGCATGAGCCACCGTGCCCGGCCAGTAT  
CTGAACCTCTGTGGCCAGGCAGAAAAGGTCTGTGTTACTCGTCTCCTTT  
ATCATTATGTTCCATATTCTCCCATTTGCTAACATTTATGTTTCTGCTCC  
ACTGGATTCTTTGGATTTTTCTAGAACATACCCATGCTTTGCATTGCCTT  
GGTCTTTGAATATTTGGTCCACTTTTCTGCAAAGTCCCCCTCTCACCTTA  
TCTTCTCGTAAACTTCCAGCCAACACCTCTTTACTAACAGAGAAACAT  
GGTTCAACTGTGCACAGGCTTGACAGAACTGTTCTCATATTGTCTTGT  
CATTGTCAATGTGGCAGAGATGCACCTTAGATACCTCTTTGAGAAAGGAC  
TCACTGCCAGCTGCCTGGCACGTGATGAGCTGATAGCTCCAGCTATAGA  
CTCCTTTAGGGTCAACCTCTGCTTTCCAGTTGAGATCATATCCTTTGCAG  
GGTGGCCTCCCCAGTGATGACTAAGGCAGTGTTACAATGGCCTAGTCATT  
TCCTCCCAATGCTGGACTCCCAATGAACCATCTGCTCCGGAGCTTCCAC  
TGGGCAGTCAGAGACCTTAGCTAGTCTGCCTCCGAATCAGAAGGCTCTCT  
CTTGCCACTCTGGCC  
>Contig12  
GCTGTGTCTAAAGATTACGGCTGTAGTTCCAACTCCCCGCCGCCCTCTAC  
TGTGTCTCTTAATGGCAGTCATTCACCATCTTCTGTCCCTCCCCTTCA  
TTTCTTGGATGGTGACTGTCACTTTGCTGCAACAGAACCCTGTCCCAATC  
CTTGATGGTTCAATACACACATAGACATTCTTTTAAACAGGGCGGCCCTCT  
CAGGTCTTTAATTTTCTTCCCTCCAATAACCTTGTGATGATCCCCAGCT  
TAGCCACTTACTGCCAGATCATTACCAGTAACCTCCAGCCCCCTCCTTAATT  
CTAGTTTCTAATATCCTAATCTGTGACCTCACATTCCAACCTCTTCATTCT  
TTATCCCCGTAGTCAAAAAATCCTTTGATCCATGCAATCCATTAAAGTCAT  
CTACCTTTTACCATTCTTCGCCCCACTAGGGTTCTCATTCTTTATTAC  
CCATATGAAATTCGAAGGCCTGTTGGAATCACTCCCTTGAGCCACTGTC  
AATACTTCTGCCCTTTTACTTCATCACCTTATGTGGCAAAACACAGC  
CCTGGTGGAGTCGATCCTTACCCCTGCTCTGTGCCAACAGCCGCACACGC  
ATGGCTGATGGAGGTTGGAAAAATCCACACATGCAGTGGGCCCTGTATGT  
CCATATACGTATCCAAACCTCCAGCCTTGCAATATGCCTCAGTGTCTGCTGA  
CAACACATTATATGTTTTCTTAGTTCTTTCAGTCTCCTGGGTGCCTAGG  
TGAGTATCTCAGACATCCTTCTCTCTGTGCAAAGCTCCAACACCTCCACG

FIG. 4 (3 of 61)

TCACATTCAACTGATGACAGTGTCTCCTATGTCACCTTAGATCACAGAGGC  
ATACATAAACAAATCCAGCCACTGCCAGCACTCTGCACATCTGCGAGCA  
TGGCACCCCAATCTAGGCCTTTCTGCTGTCACTTGGGGTGAGCTGATT  
ATACTCGATCCTAGTCATTTCTACTTATGCAC

>Contig13

CTTAAGGCCTCCCTCTAACATTTTAAATTTAAGATTGAAAAAGCAAAGATT  
ATTCTGTTTTGGCTGCGCCTATAGTAAAGTAACCCCTATGNCAAATTTTG  
ACACCTTATAGTATTTGACAGGGATAAGTATAAAATTGCTTGATTGATAC  
ATCCACACCCAAATGTATGCTGGGAATGATTTTGTTCACGGCACTCATT  
ACTTAATTTTTAAACTCTTATTTAAATTTGCAATGTTTTAAATGACCAT  
CACTTAAAGTAGTAATCAACAGAGGTTAGGAGAACATAACAATACTCTTT  
CTCTTAGAAAAATACAACAGAAATATAATTTTTTACAGTTTTGCTCCCAA  
CTTTCTCTGTAAATAACATGCCTTACTCACCTTTACAATAGGTTTGTGT  
GAGAATCTTGTAAATGTAAACCTGGGTGTTCTGTGAAGCATTTTTAACT  
TCTAGTTTACACTGACTCTTATTCAAGTGTTTTTAAAAATATATTTAAA  
AACTGGCCAGGTGCAGTGGCTCACACCTGTAATCCAGCACTTTGGGAGG  
CCAAGGCGGGCAGATCACAAGGTGAGGAGTTTGAGACCAGCCTAGCCAAC  
ATAGTAAACCTCGTCTCTACTAAAAATACAAAAATTAGCTGGGCGTGGT  
GGCGGGCGCCTGTAGTCCCAGCTACTCAGGAGGCTGAGGCAGAAGAATCG  
CTTGAACCCGGGAGGCAGAGGTTGTGGTGAACCAAGTTTGCGCCAATGCA  
CTGCCAGCCTCTGCAGNGACAGCC

>Contig14

GGGGGCGGGCCGAGTGATCCTAAAGCCCGCTCGCTTCACAACAAAGCCTA  
ACAGTCCCAATCACTTAATGCTGCATTTATTCTGGGAAGCAAGTCTCCT  
TTGCACTTTACACAGTGAGATAATCAGTTTTCTCATGTGGACCACTGGGCC  
AGGAGGGCCTGACAAAGGGCAGTCTACATTTTCACTGGAACTGCTCCC  
AGAACTATTTCTTTCTAGTTCCACCTCGGTCTGAGGTGCCTGAGGAGAG  
GGACTCAACAGAGGAAGCAGGAGCATAGCTCAAAGTCTCAGAACATGGAA  
GAGGAAAAGAATCCTCACAAGATTACGTAACCTACAGGCGTGTGTGCTGCT  
TCAGTAGAAGTTTCTCTCCCTCAATCCTGTACACTTTTCCATACATTAC  
ATACTCAAACCTGGTCAGCCCTATGGAGCAATAGCAGCAAAGTTATTCTTA  
ACAGTAATTAACAATATAAAAGATCCCATTTAAAAATGGTTACTGGTCAG  
CCGGGCGTGGTNNNTCNANCTNTAACCCCANCACTTTGGAAAGCATGCG  
GGCGATCCCAAGTCTGATATCGAAACATCTGCCTAACATGTGCAACCCCT  
CTCTACAAAAATACAAAAATATCCGGGCTTGTGTTGGCGCCGTTATCTCA  
CTACCCGGAGCTAAGTAAGAAATGCTTTACCTGGAAGCGATTTTTTACT  
TATATCCCTCTCTTACCCGGGCGCGACCAAATCTTTAGTATAGGAAAG  
TTTATTGTTTTATGCCTTTGTCAAGGCTCTACTGTATCTTTCTGTCCAC  
TCAC

>Contig15

GGTTCTGAACAACAGCAGGCGATTCTAGCCCTGTACCCGGGGCATTGTC  
CAACACTCGACAGGGCTGAATTCGTCCATAACGGTGTGCCCCCTCTGGGAT  
ATAGGATGAAATGAATTGATCTGAGTACCTGGGATGTAAAGTTACTAAAA  
CGCCAGCTAGGTTACGCCCCGATGCTTAAATATGATCGTGGCCTACACC  
TCGTCCAGCAGAAAAAGTACCCTTTCTTCAACACCACCTCAGCATCCTCC  
AATTTAGGAGCTATAAACTCATGACTCTTTATTTACCCCTGCAGATTC  
TCAATCCCAATAGTGTGTCTCCCTGTGAACTCACGGATATACCGATTTT  
CCCCACGTCATTTCCACACGTCGCAATCGCTTAGTCATCCCTATGTATGA  
GAATCATGGATGACTATGTTGAAGTCCATCTATAAAGTTCAACCCCCATC  
TCCGTCCCTGATTCCCCCTCCCCAAGATCACCAACGCGACTCGACATATT  
GTTATCGCCCCAAGGGACCTCTTGCATCCCCCATATCCACTGGTCACCTCC  
CCTCTTGGCTGGAAGTCACCGGGAAGTTCTCCACATGTTGT

>Contig16

TGCGAGCGATGTTCTTAACTTTAGCGCCATTGACTCGAGCATGGTCATG  
GCTGTTTCCTG

>Contig17

AGGGTGTTCTTAAAGGATACTACGTTCCCTAAAGTCCAGAGAAAAA  
AAAGTAACATAATGTGGCTTATTTGGTATAAAATTTTACAGGAAGCATT  
GTCAAATATGAAATAGTGTGTTGGTTTTGTTGGGCTGTATTTGTATAAAT  
ATGTTATTGGTATGTGTTCCAAAATTATAGGAACTCCTATAATTCTGAT

ATGACTTGGTGTACATTATCAGTAATAATTATAATTGTTATGGTAAATTA  
TTGTGTGCCATGGAGGTAACAAATTTCTCATCAAGTGTGTCTTTGACTA  
TGGTTGCCCTAAAACCTTTTGGCCATTACAGACAATTGTCTTGCTTTGGT  
CCTCTTTAGAAGGTGGTTTTATAATCAGCTATAAACTCTAACGGGTGCT  
CTTGAATGCAGGCTTAAGATAGCTTTGGAGACTGTGACATCAGAATAGAG  
GAAAAACTTTTCAGTATTCATGGAGTGCTGAAATATTCATGAATATCAAGC  
AAAACAGGAATTAACCTTCATAGATGGAACATAAAGAATGCTGAAGTAATC  
TTTTTGACTTTTTTTCTTAAATGTTGATCCTTCGTTTTGTTTTTCAGAG  
TCAAGGAAATTTTTCTGTTGAGATATTGACAGCTTTTAACAATTAAGTAT  
ACTCCAGTGAACACAATTTGGAGCATATTTGTGTCTCTATATATATTT  
GGAAACAATNTTTGAGTATTCTTAACCTATTGCAATATT

>Contig18

GGTTGTCTGTATACCAGTAATGGGATTGCTGGGTCAAATGGTATTTCTG  
GTTCCAGATCCTTGAGGAATTGCCACACTGTCTTCCACAATGGTTGAACT  
AACTGACACTCCCAACACAGTGTAAGCAATTCCTATTTCTCCACATCC  
TCTCCAGCATCTGTTGTTTCTGACTTTTTAATAATCGCCATTCTAAGT  
GCATGAGATGGTATCTCATTTGTGGTTTCAATTTGCATTTCTCTAATGACC  
AGTGATGATGAGCTTTTTTTCATGTTTGTGGCCACATAAATGTCTTCTT  
CTGAGATGTGCTGTCTTATATCTTTTGGCCACTTTTTGATGGGTTTTTTT  
TTCTTGCAAAATTTGTTTAAATTCCTGTAGATTCTGGATATTAGCCCTTT  
GTCAGATGGATAGATTGAAAAATTTTCTCCTATTCTGTAGGTTGCCTGT  
TCACTCTGACAAATAGTTTCTTTTGTGTGCGAGAAGCTTTTCAGTTTAAAT  
AGATCCCATTTGTCAATTTGGCTTTTGTGCAATTTGCTTTTGGTGTCTAA  
TCATGAAGTCTTTGCTCATGCCATATGCTCCTGAATGGTATTGCCTAGGTTT  
TCTTCTATGGTTTTTTATGGTTTTAGGTCTTATGTTTAAATCCTTCTTTTT  
TTTTTTTTTTTTTTTGTAGATGGAGTCTTAGTCTGTTGCCAGGCTGGA  
GAGCGAGTGGCGTGTCTNTAGGACGC

>Contig19

GCATGTTGTCTAAAGGTTTGTCTTCTCCAAAATTCATATGTTAAACCT  
AGCCCCAAATGTGATAATATTTGGAGGAAGGCTCTTTGGGAGGCAGAGCC  
CTCATGAATGGGATTAGTAGCCTTATAAAAGAGACCCCTGAGGGCTCCCT  
TGTCCCCTCCACCGTGAAGGATGCAACAAGAAAGTATGGTCTATGATCC  
AAAAAGCAGACCCCTTGCCAGGTACCCAATATGCTGGCACTTGAACCTCCC  
AGCCTCCAGAACTGTGAGAAATAAATTTCTATTTTTCATAAGCCACCGAG  
TCTATGGTATTTTGTATAGGAGCACAAACAGACTGATGTGCCACCCAAC  
CATGATTATACGTGTAATTTATGGTTTTCTCTGCTAGTAGGGATGCACCAT  
GGGGTTAGGAACACGCTTTTCTTATTTCCACACAGTCCTTAGCTCTAA  
GCATGTTCTGGAATCAAGATCCCCATCTTTTATGAATGAAGGAGTCAGT  
GAATGAATTAATGAAAGAACTGATAACCCCTCAATAATTATTCAGCCTTT  
TATACCTACTATTAA

>Contig20

ACGGTTCTCTAAAGACTTTCAAGAGCTGGATTTTATGCTTTAGGTGAAGG  
TGATAAAGTAAAGTGCTTTCACTGTGGAGGGGGGCTAACTGATTGGAAGC  
CCAGCGAAGACCCCTTGGAACAACATGATAAATGGCATCCAGGGTGTA  
TATCTGTTAGAACAGAGACACGAAAATATATAAACAATATTCAATTTATC  
CCATTCACTTGAGGAGTGTCTGGTAAGAACTGCTGAAAAACGCCATCAC  
TAACTAGAAAAATTGATACCATCTTCCATAATCCTATGGTACAAGAAGCT  
ATATGAATGGGGTTTCAGTTTCAAAGACATTAAGAAAAATAATGGAGGAAAA  
AATTCAGACATCTGGGAGCAACTGTAAATCACTTGAGGTTCTGATTGCAG  
ATCCAGTGAAGGCTCAGAAAGACAGTACACAAGACGAATCAAGTCAGACT  
TCATTGCAGAAAGAGATTAGTACTGAAGAGCAGCTAAGACACCTGCAAGA  
GGAGAAGCTTTGCAAAATCTGTATGGATAGAAATATTGCTGTCTGTTTTA  
TTCCTTGTGGACATCCAGTCACTCGTAAACAATGTGCTGAAGTGGTTGAC  
AAATGTCTCAAGTGGTACGCAGTCATTCTTCAAGCAAAAAAATTTTAT  
GTCTTAATCTAACGCTATAGTAGGCATATTATGTTCTGATTATCCTGATT  
GAATGTGTGATGTGAACTGACTTTAAGTAATCAGGATTGAATTCATTAG  
CATTTGGTACCAAGTAGGAAAAAATGTAAAGCCAGTGCTTAGACACA  
GC

>Contig21

CGCTGTCTTAAGAACTGGGCTAGGAGTGAGCAGTGAGCCAAGATCGCACC

FIG. 4 (5 of 61)

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ATTGCACCTTCAGCCTGGGCAACAAGAGCAAACTCCATCTCAAAAAATA  
CATATATATATATGACCCATAAAAAGGAGATAAATCAACACTTCAGAACT  
GACCCAACTTGCAAAGATACTATAATTAACAGAAAAGGACAGTTTACTA  
AGTACTCCGTATGTTCAACAAGTGAAAGATTAAACATATTAAGTAGAGAT  
GTAGAAGATATAAGAAGATCCAAAATGAACCTTTAGAGTTGAAAACCTACA  
ATATTTAAGATAAAAAATACACTAGGTGGGATTAAAAGTAGATTACACATT  
GCATAAGATAAAAAAAATGAGCCTGAATACAGCACAGTATAAACTATCT  
TAAACAAAAACACAGAGAGAAAAATAAATTTAGAGACTTAGCTCTTATC  
CTCTATTTGTTTCTAAACAGAGGATAAGGGGCAGAAAAATGTTTGAAGA  
AATCATGATTTTAAATTTCCAACCTGAGATAGGAATAGCACTGGGTAGTC  
ACAGGAGGCTGGAAAGACCCAAACAGCAGTTAAAACAGGAACTAGGCAAA  
GAAACCAAAGGATAACAGTAAACCTAACTAAGGGAGAGAAAACTGACAA  
AAGCTGACTTAGGATAACTGAC

>Contig22

CCTGAATATAAGCCGCAAGTAACCAATTAAATTTGTTTTCCAAAATTGTA  
TTAACAATCTATGAAATTTTATCTTGACCATAGCTATAACTCCAGAAG  
CCTTTTATAACCTCTATAACCTTTATTAAGGAGTAGGTTAATGCTTCAAG  
AAAACCTTGTTAATCTGACACAGGACCCATATGCTGATCTTGATCAGTG  
TGGCTTGGACATCAATGATTATGATTAAATTTATAGAGAAATTGAACCTAT  
TTTATCTCTCAAAATTGGCCCTTACAATCTCACACACCCACCTCTTCCAC  
TATAGTTTCTGGGCCTTGAGTTGAATAGCTTTAATTTCTGGCTCTGTGTT  
TCAAGAATGCAGTTTATTTTGATTGGCATTCTTACCAGTCTGAAGATG  
AACCTTTAATTTGCTGTGAGTATTTAAGATTTAGCAGGACTTGTCTTTTA  
AGAACCAGGAGTCAAGCCCTATAACTCAATGTCAAGGACTTTAAAAGC  
ACATACATAAAGATATATGGATGTAATAATCATAATTTTAAAAAATTGT  
ATTAATCTCAGTGTCTTCTAAGCAAACCAAACTTAATAATAATGGCATA  
GAAATTATTTCAATAAAACATAAAATCTGTTAAGCCAGTTACCAAAAGGC  
AAAAGAAAAGACCTTCTGCAATGCACAGAATATTATGTTGGAAGAAAACA  
TTTCTTTTAGACCTTTAAGAAAACATTGTTAGCATCAGGACACAACAAAC  
AGAATCTGAGGGTAAAAAACGTATATGAGCTGAAGGGAGTTGAAGGAGGG  
CATTACTATTTCCACCCCTTTTAAAGGGGAGAGAAAACTAAAAACAGCAA  
GATGCAATAAAAAGCTGAACCTTGGGTAAAAAATAATCTTAAGTCTCTT  
ATAATTTATTAAGAGTGAATCAACCCCGTAAGAAAATTTCAATGTTCTAA  
CCAATTTTATAATATAAGTAGTTTTTTAACATCAACCCCAATCTCTAGA  
AAGACCATTATAATTTCCCTTTAATTATAGACAACCTTTATCATATAAAAG  
TTTTTTTAAATAAATCCTCTTATGTGACTTACACAGACTATTATGACA  
TGCTTGGACTTTCTGGTTTGTGCTGAACATCCTTTTCTTTCTTTCTTCT  
TTTTTAAATTTTACTTTACGTTCTGGGATACATGTGAAGAATGAGGAGT  
TTATTACGTAGGTGTACATGTGCCATGGTGGTTTGTGTCACCCATTAAAC  
CGTCATCTATATTAGGTATTTTCTTAATGTTATCCCTCCCTTGCCCCC  
CACCTCCTGACAGGCCCTGGTGTGGGACATCCCTCCCTGTGTCCATGTG  
TTCTCAATGTTCACTCCCACTTATGATTGAGAACTGCAGTGTGTTGTTTT  
CTGTTT

>Contig23

GCTAAATATAAGCTATGATAAAACAGTTGGCCCTCTGTATCATGGGTTTC  
ACAACCTGTGGATTCAACTAACTGTGGATGAAAAATACTTGGGAAAAAAG  
AATGGCTGCATCTGTACTGCACAAGTGCGTGCTTTTATTCTCGTCATTAT  
TCCCTAAGCAATACAATATAACAACTATTTATATAGCATTACGCTGTAT  
TAGGTATTATAAGTAATCTAGAGATGATTTGAAGTATACAGGAGGATGTG  
CTTAGGTTACATGCAATATTATGCCACTTTATATAAGGCCCTTGAGCCT  
CCTCAGATTTTGGTATCCATGGCAGTCTGGAGTCAATCTCCTGCAACA  
TCTCCATTTGTTGAGATTCTCTTCTATATCATGTTTATATCAGAAAATCT  
ACATAAGATTTTTTAAATGTGTTTCAATATAGGTTTTGTGTATTTTGGTTGT  
TAATCCCTAGATATATGCAGTATTTATTGCTATTATGAGTAGTGTCTTCT  
TACCATGTATTCTAGTTGGTTATTGCTGACAGAGAAATGTTGCTGGTGT  
TCTAAGTTACCTTGTCTTAAACACCTTGCTGAACCTTATTAGTTCTCA  
TAGTTTTTAAATTAATCTTTCTTAGTTCTGATAACATAATCTGCAATAAT  
GACAAATTTATATCTTTCTTCCAATGCTTATATCTCTCAGTCTCTTTTA  
TCCCAAAGTATTTTCCAGGATCTCCACTATAACATTAAATAGTAATAAGA  
ATTTCTGTCTTGTACTGATCTTAAGGAGAATAAATTTAAATTTCTCTG

TCAGGTTTTATGCTTGATATAGATTGTGATATATAGCCTTTCACAGGT  
AAAAAAAAAATGCTTTCCTAGTAGTCCTAATTTTTTAAAAAATCATCATA  
AATAGATGTTGAACATTATCAAATGCTTTTTCTGCATCTATAGAGATAAT  
CATATGGTTTTTTACTATTTATTAATGTAATGAATTAGACCAATTTTCTA  
ATGCCAACTCTTCTGTATTTGTAGGGTAAATCCTATGGGATCATAAAA  
TACTTTTAATACATTGTTAGATTTGAAGAGTTAACGCCTTATTTAGAACG  
TTTTCAGTCACATCCATAAGTGAAATGGCACTATAGTGTCTATTACTATT  
ATATTTTTCTGGTCTGAAACCAAATTATACTCACCTCATACAGTAAGT  
TGGGCAACTTTGTCTTTTTTCTGAAACAATTTGTGTATAGAAGAAAT  
TAACTGTTCTTGAAGTTTGATAATAATCATCCAGAAAATTATCCCAT  
CTAGGGCTTTTACAAAAAGGAGACTCTAGAATGCCATTTTCGGTTTCTTG  
ATGTGTATTGGCCTCTTTCATTTAGGCTTTTGGATTTTATAGGCATTTT  
TTCATATAGGCTTTTTTACCGG

>Contig24

CATAAACTTCAGGTTGGATGTTCCGGTCAAAGTGGTCCGGCGATGCGAAAA  
CGAGAGGGCTCGAGGACTGGGCAGAGAACTATTTGAAGGTATCTCTCAGG  
GGAAACCAAGCGGAAGGCGGGAGTAAATTTGGAGGGAGCGACGGCCTT  
CAAAGAAGGGGCTTGATTAGATCGGCGAGATCCGGGAGGGTCTGGTGGG  
GAGAAATGACTAGAGGACAAATCTAATGGAGAGACAGACGGAGATAGATA  
TCGTGACAGAGAGAGGGACAGTGACAGCGCACACAGTGCAGGGTCCATG  
AGTACAAGGCCCTTAAGTGACACCCAGCCGGAGTCATGGCAATTCGAT  
TCCTGTACTGACCACCCAGGATTTGGGTAGACTGTACGAGTTAATGAGCA  
TGGTCCCCAACAAGACTGCTTCGACCTCAGATGCAAAGCACACTTCAGGG  
GTCCCCAAGCCACTCATGTTTTTGAATGACTGCCATAAGTTCAAAAATT  
CCCACAATTCCTCAGATTCAATAACTGGGTATAACCACTCATAGAACTC  
AAGAAAATGCTATCATTTATTATTACAATTTTATTATAAAGGATACAAATC  
AGAAGGACTAGCCAAATGAGGAGACACATAGAGAGAGGACTAGTAAAAAA  
CAGAGCTTCTGCGTCTACCTTCAAGGAATCAGGATGCACCACCTCCCA  
GCACATCAAGTGCTCATCAACCAGGAAGTTCTCTGAGCTCCAATGTCCA  
GAGATTTTACGGAGGATTCAATACATAGGTATCATTGATTAAATCATTGG  
CCATGTACTTGAATCAATCTCCAGTGTCCCTCTTCTCCCTAGAGGTCTG  
AAGGGTTGGCTAATATCATGTGGCTCAAAGCCCCAACTCTAATTACCTTT  
TTGGTCTTTTTCAGGGACTAGACCCCATCCTGAAGCTATCTACAGGCCCTG  
CCATGAGTTAGCTCATTAAACATAACAAAGACACTTATATTACTCAGAAAA  
TTCCAACAGTTTTAGAAGCTCCATGTCAGGAACCTGGGACATAGATCAAA  
TTCTTTTTTTTTTTTTTTTTTTTTTGGAGACAGGGTCTTGCTGTGTTGCCAG  
GCTAGAGTGCAACGACAGATCACAGCTCAATGCAGCTTCAACTTCCCAGG  
CTTAAGTGACCTTTCCACCTTAACCTTCCAAGTATCTGGGACCAAGAAA  
ATGGCTAATTATCTGGCTGATTTTAAACTTTTTTTTTTGTAGGGATG  
GGATCGCCCTGTGTTGCAAGGTTGGTCTCAAACCTCTGGGTTCAAGCAA  
TCATTCTGCCCTGGCTCTGTGATGGTTAATACTGAGTGTCAACTTGATT  
GGATTGAAGGATACAAAATAATTTTTTGGGTGTGTCTGTGAAGGTTTCG  
CCAAAAGACATTACTTTGAGTCAGTGGACGGGAAATCCCCCTTCCCA  
TGGGACGGGGAGACCCCCCTCCATCCAGGTAAAAAATCTAATCACCTGC  
AATGTGGCAGAAATAAAGGAGGGAAAAACGGGGACCCCTANATGGGTTA  
TTCTCCACCTAATTCTTCCCCCAGG

>Contig25

CCATGTATTTTCAATTTCTACAGACCCTGAGATGAATTTGTCAATTGCCACGG  
GGTCTGAAGTTCAAATACTCTATTTGGTATCCTGCCCCCTGTGGTTAACT  
GTGATCATTTCACTCACCTTGTTTATGATGAGAGGTGCCACCATCTGGCC  
TCCTCCACTCTGCAATCCTGTTAATTCCTATCAAAGCTGAAAACCTGCTG  
CAGCACCCACACCATCACCTCCAGCCTAGAGAGGGAAGCTACCAGTGAGC  
TCTCCTGGATGCCGGTGTGCCCCCTCGCCAATACATTTCTTCTAGTCCCT  
TGGTCATCCTGAGGTGTGTGATTAATGGACAGCTATGTGGATTGCACATA  
ATAGATGTACTCCAGCATCTTCATCCCTGATTTTCTTTACAGAAATCAC  
TCAACCTTAGCAACATGTGAAAATCACCTAAGGACATTCTTTAAATCCCT  
CTGTCCACATGGCAACACAAACCACTTAAATAAGAATCTCCAGGGAGTCA  
CTCAAGCATCAATGTTTTTAAAGCTCCAATTTAAGGATCATTACATTA  
TGTGCAAGAAATTATAGTATTTACGCTTACTGACTGTAAACCACCACCA  
TATCTAAGCATCCATTAGTCAACCTAGCAGACAATAAATAACATTACCT

FIG. 4 (7 of 61)

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CCAGGTA CTCAAATCAATTCATTG CATCCCAAATCCCAGATGGGCCCCACC  
CTTATTGACAAATTCAGCCCAATCTTGGTTGAACACATTTAGAATATATT  
TCCATGAACAATATCCGGTTGACGAGTTTCTTTAACTTTTTGGAGTTTAA  
GCCATTTCTTTTACAGTAGCCTTGTTAATCCCTGTCAATGCTCCATGG  
GGGTCATGAAGAGACCTCTTATTAAGTGTGAAGCAACTGGCTCAGGTGC  
AGACACTCAAATGCTTCACATGCAGTGGGAAAAGAGAGTGATTGTCTAC

>Cont1g26

TTTAAAAAGAACTGAGTCTTTATTTCAGTCGATTCTTCTAATCTATGAACA  
TAGCATCTCTCTCAAAGCATTTAGTCCTTCTTTAATTTCTGTCTATTAATT  
TTTTAAATTTTTCATCCTAAAGATTCTGTATATGTTTGTGTAATTTATG  
CTTAAGCATTTTCACTTTCTTGGTAACAATTATAAATGATTTTGTGTTTTT  
TATTCCTACTAGTTCAATTTTCAGTGTGTAGAAAAGCAATGAATTTTGTGT  
GTTGATCTTTGTTCCAACATCTTGCAACATTATTGAACCTCATTTATTAGT  
TCTAGGAGGTTTTTTCATTTTTCTGTAGATACCTTGAGATTTTCTATAT  
AGACAGTCATGTTGTCTGCAACAGGCACAGTTTATTTCTTCTTTTCA  
ATCTATATGCCTTTTTTTTTTTTTTTTGCCTTATTGCAGTGGGTAGAAGT  
CTAGCACTATGTCAAATAGCATTGGTGAAAGCAGACATCCTTGTTCTTG  
TCTTAGAGGAACATTTGGTCTTTAATCTTGATTTAAAAAATTCCTTGAC  
TAAGTTACCGTGTTTTGCGGGAGGGAGAGGTGGGGTGAGGTGGGGATTTC  
CCCTAATGTTTACAAGCTGGGATTTTCTTTTTCTGTGTCTAATTATTTT  
CCTCATTGGCTTGAAAAATCTGATAAAACATTTTAGGACTGTGTATAAAA  
TAGAATTAGCCAAAGCATGAGTCTTTATTTCAGAAGAAATTTTCATGGACGT  
TGTGCCTACTCTCTTGGCTTCCTGGCTTCATGGCTTTCAGATCCCACAG  
TAAGCTCTGGATAGTAGAAGTTATAGTAAGACTGACTTCTAAATAAATGA  
AGTGACTTTAACCTTACTGATATGGCTTAAAGAAAAGGAGTGGCCTTTAA  
GATCCATGAAGTCTCAAACAAAAGTGATAACGTTATCTCCATGCATATA  
TAATACTAAATATAATGCAACTGAGAGAAGTAGGCTGTGGTAAGAAAGGA  
GACCAAGTGCCATCTGAAGGCAGCACTTACCACTCTGCTTCATCCCACC  
GAGGAACAAAGCATGAGTATTGCCAGATTTTCTTCTGTTTCAAGAAAAG  
CCAGAAATCCAGGTTTTTGGCGTGAAATGCTCTGATTTTAATGTTGGGAAC  
TAATTTATATTTTGAATAACATTGTGTGGGACAAGTGAACCTGTATGTG  
GAAGTGTCTTCTCCAGTGGCGACCAAGTTTGGACCGTTGATACTCAGCAA  
GTTTCAGCCAAGTGCGCCTTGTCATTGTGAGTCATCAAGGTGATGTGTGAT  
TGGTCAAGCAATTAATTTTGCTCAGCATCTCGTGTGTTTTCAAAGAAGT  
GAAGGTTCAATTGC

>Cont1g27

TTTCAGAGCACAATGCGTATTTCATAGTATATTGACTTAATTTCTAAGTGT  
AAGTGAATTAATCATCTGAATTTTTTATTTTTCAGATAGGCTTAACAAATA  
GAACATTCTGTATATAAATGTGTAAATTAGAGTTAATCTTTCCAATCACA  
TAATTCGTTTTATGTGAAAAAGGAATGAAGTGTTCATGCTGGTGGAAAG  
ATAGAGATTATTTTAGAGGTTTGTGCTTGTGTTTTGGGATTCTGTTTTT  
TTTTAAAAATGTAAATGTACTTGTGTGAATGATTTTTTAAAAATGATT  
TACCATTTTTGGAAGGGTATTTAATGATAGAATATCATCGAGCCAACATG  
CACTGACATAGAAAGATGTCAAAGATATATTAAGTGTAAAAATGCAAGAGG  
GAAAACACTATGTACAGTCTGAGCCAAATCAAAGCATGTATGTTTTTTAT  
ATGTGTACAACAAAAGGTTTGGAAAGATATGCGCCGAATTGTAAATGTG  
GTTTCACCTGAGGGGGTGGGAGGATGGGGCCCCAGAGGGGTTTTATGGG  
GGCCTTTTCACTTGGTATTTTTTTTCAATTTGTTCTGTTTGAAATTTTGT  
TTTCTTTTTTAAATGGAGTTTCACTCTTGTGCGCTAGGCTGCAATGTAGTG  
GCGTGAACTCAGCTCACTGCAACCTCCGCTCCAGGTTCAAGTGATTCT  
CCTGCTCAGCTCCCATGCCTCCTGTGTAGCTGGGATTACAGGCACCCA  
TCACCATGCCTGGCTAATTTTTGTATTTTTCAGTAGAGATGGGGTTTCACC  
ATGTTGGCCAGGCTGGTCTGTAAATCCTGACCTCAAGTGATCCACCCACC  
TTGGCCTCCCAAAGTGCTGGGATTTTCAGGTGTGAGCCACCACGCCAGCC  
CTGTTTAAATTTTTATAAGTATGTACTACTTTTGTAAATCAGAAATTATTA  
GAAAGCATTTTACTGATTTTAAAGCTTAGACATGTTCAAATGCCTGCAAA  
ACTACTTAACACTCAGCTTTAGTTTTTCTAATCCAAAAAGCCGGGCAGT  
TAATCTTTTTTGGTGCCAATGTGAAATTTAAACGGTTTTATGTTTTTCTG  
TGTTGTGAATGAAAAATATTTCTGAGTGGTGGTTTTTTGACAGGTAGACC  
ATGCTCTGTCTTGTTCAAAATAAGTATTTCTGATTTTGTAAATGAAAT

ATACAATATGTCACAGATCTTCCAATTAAGTAGTAAGGGTTTATCCTTAA  
TCCTTGCTAATTTAAGCTTGCATAAGTCACTTTACTAAAAGATCTTTGTT  
AAGCTAGTATTTTAAACATCTGTACAGCTTATGTAGGTAAAAGTAGAAGCA  
TGTTTGTACACTGTTGTAGTTATAGTGACAGCTTCCATGTTGAGGTTCT  
CATATCACCTTGTATCTTGAAGTTTCATGTGAGTTTACCATTAGGATG  
ATTAAGATGTATATAGGACAAAATATTAAGTCTTTCCTTTACCTAAGTTT  
GCTTTCTTGACTAGTAATAGTAGTAGATATTTCTGTAATAAATGTTCTCT  
CAAGATCCTTAAAATCTCTTGGAAATTATAAAATTATTGGAAAGACAAGA  
ACAGTTTTTATTCAATTATATGCATTATTATCG

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CTTTCTCAAGAAAAAGGGAACCTGGAGCAATTAACATATGTAATTTTTTTT  
TAAAAAACCTTAAACCTTAAACATCTACCTATATACAAAATTAATTAACA  
ATGGATCATGGACTCCAATGTAAACATGAAACTCTAAACTTCTAGAAAA  
AAAACCTGGAGAAAACCTTTGGTACCTATGACAAGGCACAGTTTTTAGACT  
TAACACTAGAAGTGTGAACATATACAAGAAAAATTAATAATTTGAACCTT  
ATGAAAATCAAATTTTGTCTCTCCAAAAGACCCTGTTAAGAGGATGAAA  
ACTAAATTACAGATTGAGAGAAAAATTTGTAAATCACATATTTGACAAT  
GGACTTGTATCTAAAATATCTAAAGAACTCTCAAAACTCAACATTAAAAA  
AAATATCTAATTAGAAAATGAGTGAACATTTTACGAAAGGGCCTTATAG  
ATTAGCAAATAAAACACTTGAAAAGATACTCAGCATCACTAGCCATTAGA  
AAAATGCATATTAACCACAATAATGTATCGCTACACACATATAAGAAT  
GGTTTATGAAAAAATAGTGATGACACCAACTGTTAGTGAAGATGTGGAGA  
AACACTCATACATTGCTGGTAGAAATGTAAATGGCATAGCCACTGTGGA  
AAATTATTTGGCAGTTCTTTTAAAACTAAAAATCAATCTACCACACAAC  
CCAGCAATTTTCATTACAGGGCATATATCCCAGAGAAATGAAGATTTATGA  
TCACACAAAAATCTGTACACAAATGTTTTATGGTCACTTTATTCATAATA  
GCCAAAACCTGGAAACTATCCAAATGTCTTCAATGGGCAAAGGATTAAA  
CACACTGTGATACATCCATACCATGGAATACTACTCAGCAATAATAAGGA  
AAGAATTACTGCTACACACAAGTTGGATTAACTCAAGGAAATTTGTGCTG  
AGTGAAAAATTAACAAGCCAATCTCAAAGGACACATACTTCATGATTCCA  
TTTGTATAACATTAAATTAACACAATTAATTACAGAGATGGAGAACAGAAT  
AGTGGTTGCCAGGGATTATACATGGTGGACGCGGTGAGGCGGGCCTCCAC  
GCCTTGGAGATGAAGGGGGCTACACCCTTTAAAGCACACCCACGAGAGAG  
TTTTGTGCGGAGGGGGCCCAATTTAAGTACTCCGCCCCGGGGGGGGAACAC  
AGGGGCAAAACAAAAAAATTTGGCCTTGGGGGTGACCAAAACACAAAAAA  
AAAACAAACACACAAAAAAACAACNATGGGTGGGAGGATTAATCGCCAAA  
TCTGAGTAAGCTATCTGGACAGTACCAATATCGATTTCCAGTTTTGATG  
TTGTACTATAATAATGCAAGATGTTAACATTGGAAGAAGCTGGCTGAAGG  
GGGCTCAGGAACCTCTCTGGACATTTCTTTGTACCTTCTGTGAATCCATC  
ATTATTACAAAATAGGACATTTTCTAAAGGTTAAATCATTTTAATTTTAA  
AATGTCCCTGTTACTGTTGAAACTCACATCTCCATATACTGATCAAGAAC  
AGCACTAATGGCCCCCTGGCCTCCAGGAATTCACAATTCCTACTGACTTTT  
CTTTGAAACCTTGGCCAAGTCGCTTCTCTTCTCTGGTCTCAATTTTTCA  
TCTTCAAAATGAAGATTGAATGACTATTAATCTCTTGCAATTCTTGAG  
ATGAAGGGTCTTAAAGGAACTGAAGAGGATGCCATGTAATGTAAATATGG  
GTTTTTACTCCATCAGCCAGCCAAGACAGAGGGCAGACACCAAGACATGG  
TAACCAAGGAGGCCATGTGTAAACAAAGACCATTTAGACTTATGCTCTGG  
CCTTTGCAGCCCAACTGGTGTGGCCAGTTGGTGGGGTATGAAGAAAATGG  
GGCCTTCCAGGAACCATGTTGAGTGGAGATAAGCAGGGAGGAATGCAGAA  
GACATGGGGCAGTGCCAGTCTCAGCCCGAGCCAGCTACCCACACATG  
GTTATGAAAGACTGACAGCCTGTAAGNTGAACACAGCCCTGCCTCTCTTA  
GATAGGC

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GCAATATGATCTCAGATGTGGATTTACTGTAAAGTTCATCAAATTTAAA  
TTTCAGAACACTTAATCTGCAAGAGTCTTTCCAAGACCCTATACCTAAT  
TTTGTGTTTACAATTTTATATTTGTTTCTTAAAGAAGACCACCAATATA  
AACTATATCCAGCCTTCATGATAAGTACATAGGAACTATGCAATAAGG  
GGGAAAAAAACAAAGAAAAATACCTAGTTTACTAATGGTTCACCTCTGA  
ATAGCACATATTCATAATGATACAAGCACTCATTACTAGTCTAGGAAAAT  
GAAGATATAATTGCATTAGGAAGATCAAGAGGTAGGAAATGTGGATGTGT

FIG. 4 (9 of 61)

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GTGGTATAGACTAGGGCAGGACAAAGAACCTAAATCCTCATTTTCTAAAG  
ATAATTGTTAATACGTAAAACTCAAAATTCAGGAAGTAACAGTAAAGCG  
GTCATTAAGAAACAAGCACTAAACACCAGATAGGAAGCGAGAGATGGGGG  
AAGAGGGCGACAATCTGATTATTTTTCACACAAATTTTGTAAACCATT  
TGACTGTTTACATGTAGAACTTGGATCTTTTAAAAAACACAAAATAAT  
AATACTATTATTTTAACTGGATTTTGAAGAAAGATAAAAGTCTCA  
TTTAGTAATTAAGACTCATTCCAGGTTAGTCCACTCAAACTTATATTC  
GAAATTAAGAACTTTGGGAGGCTGAGGCAGGCAGATCACCTGAGGTTGGG  
AGTTTCGAGACCAGCCTGACCAACACGGAGAAACCCCGTCTCTACTAAAA  
TACAAATTAGCTGGGCGTTGTGCATGCCTGTAATCCCAGCTACTCGGGA  
GGCTGAGGCAGGAGAATTGCTTGAACCCGGGAGGCAGAGGTTGCAGTGAG  
CCGAGATCACACCATTGCACTCCAGCCTGGGCAACAAGAGTGAAGCTCCA  
TCTCAAAAAAAGAAAAAATTAAGAACTCTGGAAGTTGAGTTTG  
CAAATATTATTATTTTAACTTGTATGTTTGGAAATGTCTATG  
ATGAAATTGAGGTTGGGGATGAGAAAAAAGAAAAACATCAACCCAC  
AGCCCATTCATTTTCAGCCCGACCCACAGCTCCGGGGAAGGACAGCAGG  
TCCATCCTTCACTCTTTCTTACCTCTTCCCTCCTTCTGGCTCTTCCA  
CCTCTAATTTGGAGCCCCAAAAAAGGCAGTGGGAAATGGAAAGTCTTTT  
GTACGTGGTACTTGCCGGGGAAGCTGCCATGAAACCTGGCCCCACGGTG  
GGGAGGGATGCCANCTGAGGCCTCGTGCCCATGCTAGGATAGACTCGT  
CCAAACATGTCCCGAGGAGAGAGGCTGACAGGGCAAGCANGAAATCATGTATG  
AGTATGAAGTATCTGTATGCAAGGGCGGGGAGAACACGCGGAGGAATGG  
GGCGTGAGAAAACAGCACAGTACGTTTCTTTAGCAGCTGTCTCTGCTCAG  
CCATGGGAGGTACAGAGAAAGAGGCTTGGAGGCGTTATTTTCACTGTGA  
GATGTGAGTGTAAGAAAGTGCCCAAGACACAGTGAGTACCAGGGAGATGC  
CCTCTTTCTTACCCGAATGCAGAAATGGCCACAGGCCTTAAACACACACA  
TGGGTCCCTCAGAGGAGAGAGGCTCCACAGTGGACACCCGATTCTCCCC  
TGGTCAGCAGCAGCAGGGGCGAGTGCTGGGCCATCATGAAGCTTACAGGC  
AATGAGCTCTCAGCAATAACAGGAACAGTGCCCTGGGGGACTGTAGCTGCA  
AGACCGATTTTTCATGTAAGATGGCCTCTGAGGACTCCGAGATACACCAGG  
CTGAGACTAGCTGGCAGCTCCAAGTTGTTGGTCAGAAGAGAACAGGAACT  
AGGGAAATTGGAATTACTGTTACTACAATTCCTTTACATCCGCACAACCA  
TGAGGTCCAGCGATTTTCTATTATTTTTTTTTTTAAGACAGGGTCTCAGT  
ATGTCGCCCAGCATAGAGTGCAATTGATGTGATCATGGTTCAGTACAGTAT  
TCACGTCCCAGGCTCAAGTGACCTCCTGCCTCAGCCTCTCAAGTGGCTG  
GGACAGCAGTTGCATGCTACCAGGCCAGGCTTTTTTTTTTTTTTTTTTA  
GTTTCTGTAGACACATAGC

>Cont1g30

GGTTAAACAATGGCACAGGGAAACAAACAGTTCCAGGTGCAGGGGCTCTAA  
ATCTATATCAAGATGTTAGGTATGGGGGCTCTGCCGACACAACTCAAG  
GCTTTATGCTGTTATCTCTTGAGCGAAATCCTGGGAACCTTCGTACATTGC  
TTGCTTCAGTACCTTATCAGTTAATCGGACTCTTTGATATGTTGGGAGTC  
AGCGTACACAAGTTAACTCCTTGAGGAAGGGGGTGGGTAAGGAGTCCTTG  
ATGTCTGGTAAATGAAGGAGCGAAATCGAGTTCCTCTGGCTTTCTCAGCT  
AAGGGAGAGCTTATTCATGTGGAACAAGGCTAAGTGATTAAGGGAGAAA  
GGGAGAGTCTGAAAAAAGGTTAGGTATTACAATGTCAATAAAATTGGTC  
TCCTTATACAGTCCATAGGTAGATTCTTTCCATCTTTAATCTCCCTCTA  
GCACCACCAGACTTTTTCTCTGTACCTTGAGATGTAAATTTTGCTATC  
TGAATTTTCGTCTAAGAGTTGTTTCTTTAATATGCAAATTTAGGGTTAT  
TTAGCTGACAACTGCCAAAGTAGTGAACAAGTTATCAAGAACTTGAACG  
TCTAAGGTAGGAAAAAAGTCTTTATGAATCTATAAGATGTACTTCT  
ATTGGCATGCCTAATACGTCTATGTATTTACGTGTTGTGTACACAGTTT  
TCACTACTGAAAAATATAGAGGAGTTCTAATTAATTGACTTAAGACAAT  
AAAAGCGCTTGAATCAATACCTTATCAGGAAAAAGGAAAGACAAGTCA  
AATGCTTGTTCAAGTTTATATACTTAAGTAAATCTTTAATAAATAAGC  
TAGCTTTAACATTATTTGAAATGTCTTAAGAATTGCCAGCAGGTTCTGGG  
TTACAGAACTAGTGGGGGTGCAGTGGGGTGAGGGTTGGTGGGGTGGGGG  
TGGTACGGGGGCTTTGTTTTTCTTGCTGCCCCCTTCTGGGTTGGGGAAG  
TGGCAGGACCTTGGCAGCACCCCGAGCCGGCATGGCGTTAATAATGGAGG  
GATGCCAGACCCAAGTGCTAAGGCCCGGCTGCAGAGCCAAGTTGGCATT

FIG. 4 (10 of 61)

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TCCAGACTGGGGCTCGGGCCGCACCCTCTCCAGGACCCCTCCCCTTGTACC  
GAGCAGATTGTGCGGGGAGTTTGGGCCAGCTGTCTGGCGTGGAATTTTC  
CCAAATTCAACAAATCCTCCAAGAAATCAATCCATCCATTCCATCCATCCA  
TCCATCCATCCATCCATCCATCCATCCATCCGTTGGCAGATTATGAAGCAT  
GGATCATTACTTTTGGGATGTGGATATATTCAAGTTAACAGGAGCAGCTT  
TCAAGAGCTGGATTTTATGCTTTGGGTGAAGTTTAGAAACACTAGCTCCC  
AG

>Contig31

ACCTCATGTGCTCTAGCGCCTCTTACCTCATGCCCTCCACTCTCAGTCTT  
GCACTCACCTGCCACACTCAAGGGCTTCCCCAGGTTCTTCTTAGATTTC  
CACCGATAGCTCAGGGACTTTGCACATGCTACGGTCTCTGCCTGGCTCCT  
CCCCAGATCTTCTCATGCCCTAGCTGCTTCTCATCAGCACCCCTCAGAGAC  
TGTCCTTGGCCACCTCTCCAGGTTCCATACCTGCCACCCTCCCCCAATC  
ACGTAACAGTTTCTTCAAGAGCGAGTTACCATCCAGTATTTCCCTAAC  
TTATTTTTTGTGACTGGTCTGTGCTGTCTCCACCACAAGAACATAAGC  
TGCAATGTGAACAGGAGCCTTGTCTATCTTGTACCCCACTGCTGTGACA  
TAACCTGATACACATTAGATGCTCAATGATGTTTGATGAATGAAGTGCTG  
GTAGTCCAAGTGTGTTTCTTGTCTGTGTAAGTATGTCTGTGTGGTTTC  
CTAAGAACCCTACAGCTCTCCACTGTGACTCCTGTTCTATGGTCTTGATT  
TGCTGGACTAGAATCCTAACCTACATGCTTACTCTTAGTGCTCTCCCCCA  
GAGGCTGAATCCAGTCCCTAAACCTCCACCAAATGGCTAAGACCTAGCT  
TCCAACCAGACAGGCTACGCTGAGACCTCAGCACCGCCCTTCTGCGGTC  
TCATCCTTAAACGCATCCTTCAAGGGCCAGCTTAAATGTCTCTTCTCCAAG  
GAAGGCTATCCTCTTCTGCCCCCTCAGTGCTCTCCATGCCTCCTCTATGC  
CTCCATGCCTGCTTTCCAACCCTGCAGAGGTGGAGAAGTTGCTAATCTGC  
TGTGTTGACATGTGCTGGGGTGCCTTGGGCCAGGGAGCAGGCTGGTGGTG  
TGCTGATAGCCCGTGGCTGTGCCAGGTCCATGCTCACTTCTGAGCCCC  
AGTGGAGTAGGCTCCCTTTCCCTTATTGCAGCACTCAGAGGAAGGACGTG  
CTTCTTAGGACAGATCTGGCCAACCTCTCCCTCGTGAGAGAAGGCCCAGC  
CATCCTCTTGGCCCTCTTCTTCTCTCTGCCCCGAGTAATAAAGGTGCCT  
GGTCAGAGCCTTCTAGAAGGAGACCCAAACATCCACCACACATTCCAGT  
TCCAACCGTCATCCACATGGCTGGCTGTGCAGGTAAACGCAGAGTCTGTT  
TCACACACCCCAACCATCTAGTATTGGATGGGAGGACAGTAGCGTGACACT  
CTTCTCCAGCCTTGAGCCCTACTGTGGGCCCCACCCAAACCAGATACCAG  
AGGAGCCCTGTACTGGGATGCTATTGGATGCTTGTCCAGTCATGTACAAA  
GTTAGCCCTTTGTTATATAGAGTTAGCTACGTACATCTTCTCTGTAGGG  
AACCCTAAGAGGGGAGAAGAGATATGTAGTAGGATTTAACTGCAAATCCT  
CTGCTGAGCACCGTGCATACATACAGTGGGTAGCATGTGGTAGGTGCTC  
AATAACTATTGACCGATCTATTGAATACACGTAAGATCGTGACACTATCT  
AAAACGNGGGGTGTGGGGGAAAAACCCCCCTTGTTTAGGAAACCCAAA  
TTGGACCGTGTGGC

>Contig32

GCGCGATTGTGCTAAAGATCATGCATGCCTGATCAAACGTCCCCATATGG  
CGTCTCAGAGTCAACTCCTTCCCCATCAGTGCCCTGACTTCGGCATAACA  
AACCTGGCAGGTTAAGTGATTAATCGGTCTGTACAACTGTAGCCCTTAG  
CAGGAAGCACTAAGCTTCGTTTTCAATTTATTTCTTCCCTGGAACGTCAAG  
AAATGAGGGATGCCTTCCGCCATGAAGTTTGTCTGATTGTCCACTTTGTT  
CTCAAGGAGATATTACAGTTTTTAATTTGTCTTTCTCTCTGCTGCTGCTC  
TCCAAACCTGTCCAAAGAAGCCAGCTGGCTCCATCATCTGTAAATCACC  
ATTGTACCCAGAGCACTTGACTTCTGTTGCCCTACAATCCACCTGCACT  
TTATTTCTGCCACCATGATAATGTAGTGTTACTACATTTTACATTACAGC  
TGTAAGAAATGTTACATTCAATTTACTTAAATCAAATTAAGTCTGCTCACT  
CAGTCCCCCAGTGACCAACTTATAAAGAGAAGGTACATTTCAATCAT  
CACTGAGGTTCTCTTACCACTGGAAACTGAGGAAGGTCTGGAGTCCA  
CAGTGGTTAAACATCATTTGCCTCTGTTTTTCTCTCTCAATGTAACCAT  
CCAAGGTTACTACAAATTCACAAAAAGAGGTCTTCACTCTGCTCTCAA  
GACCCAGAGGGCTGGGTTCTAAACTCAAAGGCCAATGTTCCCCAATTTT  
TGCATTGTTTCAACATTGGGGAAAACTCGAGGGGATTCAAGAAATGGTTAT  
ATAAGTTTTGTGGAAAAATGTATAATTTTTTAAATTAATAACAAAGTA  
TTATGGAAAGCACTAAATATTGAATTTATATAAATATTCCAAATTTTTT

CTAAATTTTGTAGTGAGAACTTGAGCTTGCTTCTGTGAGATATTTATTTT  
AAAACAGATTTGACACTTAAAATGTCTAATCAAGCCTTTTAAACCATGAT  
CTATCTCTTCAAATTTCTTCAAGATGCCACCATCAATAAAGAACTTTGTTT  
ACACAAGTAAGTGGTAGCAAATGGCAGGGTGTATCATTTTTTTTTTTT  
CTTTTTTTGAGACGGAGTCTCGCTCTGTGCGCCAGGCTGGAGTGCAGTGG  
CGCGATCTCAGCTCACTGCAAGTTCCACCTGCTGGGTTTACGCCCTTCTC  
CTGCCTCAGCCTCCCGAGTAGCTGGGACTACAGGCACCTGCCACCACGCC  
CGGCTAATTTTTTTGTATTTTTTAGTAGAGACGGGGTTTACCGTGTAGCC  
AGGATGGTCTCGATCTCTGACCTCGTGATCCGCCCCGCTCGGCCCTCCCA  
AAGTGCTGGGATGACAGGCGTGAGCCACCGCCCCCGCGCTGTTTATCA  
TTTTTTGCCTGATGAAATTTTCTTGCCACTACTCTGGATGGTTTGATAC  
ATTTAAATTTGTGCTTCCAGGGTACAATTATCTTTAAATCTATACCTCTT  
TCCTTTCTTTTATTGACAAATATAATGTTACACTTTTCTGTCAATTGCAGC  
CACACCACAGTACACAGATCCCAACAGAGTTGTAATATTTATTAGTTT  
CAGAGTTTCAATATTTTATCACTTTCAATACTTCATGTGCAGGAGTTTFA  
TTTGGTACTTCTTTACAAATAAATGATGTGCTTCCAAGCATTCTTTTC  
AATAATTTCAATCAATGTTATTAACTGAGTAATACTAGTATCTGTTTATT  
CATAAATTTACAGGAAATGCTTTTTTACTTATTAGTCTTTGGAATCTGT  
TGTTTGTATAAACATCTTTTATGATGGCTTTGTGTCTACCAATAGCACTA  
TTGCCAAAAGGCACCTTTTTCTTGTCTTTACTTCACTGGTCCGAAGCC  
TGGTACCAACAACACTACCACACAGACTGGGAAATGAGCAATTTTGCCACGT  
GCCCTTAGCTATTAATGGTGGCACTCCATACTAGCATCTTAAGCTCAAT  
TTCATGAAAGAAATGTGTTTCTTATTTTGTACTTGCAGGCATTTTTAAA  
CTTGTAATCTTTTATTCACTTTAAAATTTAAACAGAGTAATAGAACCC  
ATAGAAGGAAATCAATACCCACGAGTCCATACTGATATAAATAAATAGTT  
ACATAAATAAATGGGGGGAGAAATAACAGCTCTTCTTACAGAAAAATTT  
CAATTAATAAATGAAGAAGGAAATTAGGGAAATACAACGTTACCATTAAGC  
AACCACAGTAATAATCATTACAGGCAATATCCAAAAATAAATTCCAAAGC  
CAGTGGGCAAAAGTTTGAGGAGATACAGGATATTAACATAGTCTCAAAT  
AGCTCATGCTATTTATAAATTACAAAAGGAAACATAACAACCTGTATAGTG  
AAGAACTCAGCAGACACACCTTAGCCAAGTGATCAAGGTTAACGTCAC  
TAGTAATAGGGCTTGTGACATACTGGACTCCAATCTGATACACTGATAA  
GGACACATGACTTCTGCAGTATTCTTACCAAAAACAGAAATCTAATGTAA  
TTAAGGAAATGTGAGACAAACCTATTCTGAGAAACATTCTATAAAACAA  
CTAACCAATACTTTCAAATTTGTCAAGGTCATAAAGACCAGGCGATGGTC  
ACAGATTTGAGGAGACTAAGGAGATACAACAATAAATACACAAATGGAA  
CCATGGCATTCTTGATTGGATCTTGAAACAGAAAAAGGATATTAGGAAGA  
AAAGCTGATGAAATTTCTAATACATTCTGTAGTTTAATTAATAGTATTGTA  
CCAATATTAATTTCTAGATTTGATCATTATACTATGGTTAAGTTTTTAA  
CATTAGAGGAATCTGGGAGAATGGTATATATGAACCTCCACTGTTCAATTCA  
ACTTTTTTCAGTAATATTATTTCAAATAAAGTT

>Contig33

GGGAGCGGCGGCCACGCTGATCTCTAAAGCTTTAGACCACATTGGCTCG  
AGCATGGTCATGGCCGTTTCCTG

>Contig34

GACGTCTTAGCGCTATATTATAAAGAAATATTACCTCCCTGCTGAGCTT  
ACAGGGTGACCTAATGTCCAACAATATGAAATCTCTTCAATGAATTGCA  
GCACGTCCATATATAACCCACATGGAAGCTGTCTCTTTCTCACCTTCG  
AACTTCCCATGCCAAAGAGGGACCTCTTGGACTCAAATACATCTTAGCAA  
TATAGAAGATGCTGGAGACTTGTAGGAGAAGTGGAGAGGGTTTACAGTGT  
AGCCCCACAGAAAAACCTTATGACCCCATCAGTCACTTGTCCCTTTTTT  
CCATGCCTCAGTCTAGTCAGGAAACCACTAGATCTGGATGGCTTCTTCT  
CCCTTCCCCTCTTTCTCTCTCTCTCCCTCCCTTGCTCCTCCTTCTC  
CATCACCCTCTCTTACTTCCAACCAAACTTGACTAGCTCCAGTCTCAT  
CCCTCCTTATTGAAAACCTATTTTACTCAGCCCTCCTCCCCACTCCTGCC  
CAATCTTTATTCTTACCTACATCAGACTTCACCAAAACAAAGGCCAGGA  
TAATAAACAGGACAAACTCTTTCAAACACATTTAATGACCATATTTTGT  
TATTTTGGTACAATTTGAGGAGTCCCAATCCCAGGGAAGACTAACAAGA  
AGTTCTCTTAACAAAGGTGGGTCTCCCTTACTAAAAACTCCTGTAATGG  
CTGAAAAGAGCATGAGGTTTTCTGCATATCATTACACATTCAATAGAACG

FIG. 4 (12 of 61)

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TCATGCAGCTGTTAAAAAAGATCTGTAGAGGCTATCTTGTGACAGAAAG  
GCATTGGAGATATACTGTTAGTGACAAAAATAGGTTATAAATGAATTTTT  
CCATGCATGCCCTCTATATTTATAAATACACACACATAAAAGACAGGAAGG  
ACAGACATTAACATTATAGTGTCTAAGATGATGCATAGTATAATAGTT  
AGGACCATGGCCTTTGGGACAGAAACTACAGCCTCTCTCCCACTTATCA  
GCCATGGGACCTTTGGGCAATTTGCTCAGCCTCAAAGCCCCTGTTCCCTTA  
TCTGTGTGCTGGGGTTGTTGTAAGAGTTAAGTGCAATACACAGAGAGAGA  
GAGAGTACCTAACATGTATTATGTGCTCAGTCAATATGCATCATAGTACT  
CATTGTTACATATGTTCCCTAAGTGCTTTATACGTTTTTCCCTAAGTTGA  
CCATCTGTTTTTGGCATTATGAAACATAATGATCCTAACAAATTAAAAAT  
AAAAACATAAAGAATATTTGCCCAAAAAAATAAAGAACATGAATTCCTC  
AAGTAGCCCAAGGGGCATAGACAGAAAGTAAGCCCTTGGTGGGGCTTAGTT  
GAGAGAAGTCTCCAGAAGGTCTTTCGTGTGTTAAAGAAGAGGGTAACAGG  
GAGGAGGTGGGGAGAGATGTTAACTGAGTCTAAATGAGCACCTGGAAGAA  
GAGATGGGACAGGCCACTTCTGCCTGGACTCCCTGATTGTTAAGAAGAAT  
GAAAAAGAGCAGAAGTCTTCCCTGAGCCCACTTCACTCCCTGACTTAAC  
CTAGTCTTTGCCCCCTCCCTCTCACTCATGGCTACTTTCTGTGGTCACCT  
TGTTGTAGAAATGGATGTGACGCCACCTCATTTTTCTACCTCCTTCA  
ATGTTTTTAGATAATTTAATGTAGTAGAAGACGGTTACAGCAAAAAATTAC  
AAAAATCAAAATATCTCTGCTATCTACTGTTGCATTTCTAACCATCCCAA  
AACAGTAGCTGAAAACAGCACTCGTGGTCGAGCGCGGTGACTCATGCCTT  
TAATTCAGATACTCCGGAGGCTGAGGCAAGAGAATCACTTGAACCCGGA  
AGGTGGAGGTTGCAGTGAAGTCAAGATCATGCCACTGCACTCCAGCCTGGG  
TGACACAGTGAGACTCCGTCTCAAAAAAAGCACTCGTG  
TATTTTGTTCAGATCTGTGGTTTGGGCAGGGCAGGGCTCAATGAGGACA  
TCTCGTCTCCGTTCCCGCAGTGTGAGGAAGTGAAGTGAAGTGAAGTGAAGT  
CACACAGAAGATGGCTCCCTCAAGTGGCCAGCAAATGGTGCTTACAAT  
GACAGGGAGCTGTTGACCAAGGGCCCCAATTCCTCTTCTATGGCCCCCT  
CTCGGGCTGCATGGGCTTCTTTACAGAAATGGCAGCTGGATTCCAAGAGCA  
AGTATCACAACTACAGAAGAGTGGAGGAATATTGAAAGTTACAGTCTC  
TTAAGACGTTGGCCAGAACTGGCAAAAGCTTCATTTCTGCCATGTTCT  
ATTGATCAGTCACAGAACCTGCACCAATTCAAGAGGAGAACATATAGAGG  
ACATCTCTCAATGGGATAAGTGTCAACAAATTTGCATCTATCAAACTG  
TCTTTTGGGTACAACTATTTCTATTCCTCCATTATGCAAAATATACTCA  
CAACCTCCCAGGGGTGCAAAAGCCTCATCCATTTATGGCAAATGTGGCC  
CTTTTAATTTATATAAAATAATTTGCGGGGGCTTCTTTATATTTTTAAC  
TCCCCTGC  
>Contig35  
GTGCAGAGAAGTGATTTAAAGCCCTTCAGAAAGAATGCTTTATTCCCGTG  
GAATTTGGTAACCTTGCTTGGGTGTGGGGAGGTTTGTGAGCTTTCTCCACT  
CAAATTATCAGACCTTTCCATTTAGTGGTAGACATTTCCCTCGTCCAG  
GCCAAGGGCACATAGTACAGAGAAATAGGGAGTTGTTACCCAGGGAGAGA  
ACTTGGCTCTAAACCTGTAATAGAAAGGTGAGTCTGGTCTGGAGGGTCA  
ATTTTGATCTTTGGCTCAGATCCAGGAATTGGAACCAAGGCTTTTGAACA  
TTTTAATGCAGGGGATTAAAAAATGATACGAGTCATTACGAAATATATT  
TGCTTAACATCTAAAGAGATCCCTCAAAACACTAGAAAAATAAGAACAA  
AAATCTAATAAAACAAAATTTGTTAAACACATTTACCAAATTTTTTTTTT  
TGGTAAAAATTCAAATGTCAATAAATAAGCTAAAGTTCCTCTTGATGACT  
CGCTCCTCTGCCCTATTCCACTCCAAGTAACCACTATTATCAGTCTTGCC  
AATACCCCTCCAGACCTCTCTACCTCTATATACCATTAGAAGCACATGGT  
TTTGCAATTGAGGATGTGAGTGTGTTTGTGTTTACGTAAATGTTATCACTCT  
GTTCTTGTTCATAATTTGCCTTTTTCTCTCAATGATTGCTTGGCTATC  
TTTCTATTTAGTAGCATCTCCTTTCTTTTAACTTACCATTGTTTATTT  
AACCTTGCCTCTATCAACAGATATGTAGGTTGTTTCTAGTTGATTTCATT  
AAGTATTTATAACAACGCATCAGTAGATGTCCATAAATTTCTTTACGGA  
AGATGGCAAGTAGTGAATTTGCTGAGCCAAAGAACATGTTTAAAAAACC  
AAAAAACTAGACGCTACCAATTTCTCTCCAAATGGCCATACCCACTT  
ACCCATACAGAGATGATTTGGAATCTGGCTTCTCACAAGGTGAGATGCC  
TTCACAGTTTCATTCTTCTGGCATGTCTCCCTTTTGTATCTGAGAGAG  
CTGGCAGAATTTGTGCTACTAAATCAAGGATAGAGGGTCAAATGACAGCTC

FIG. 4 (13 of 61)

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AAGCTCACAGGCACCTCTGCTTTCTTCLAGACCACCTGCTTTCTGCLA  
CCAGCTCTGTTCCATCTTATAGAATGGTTGCCACTTGGGTGTCTGCTCCG  
ACAGCCATGTCTATCCTTTGCACTGCAGTTATGAAGCAGACAGAGCTAGGA  
GAGGGGCTTTGCCAGCCTCTGCCCTAGCTTGGAGAACTTCAAAAAAGGAG  
GGTATTGAAGTTGAACTCCCCCAAAAAGGGGTGGTCCCCACACCTCAAAA  
AGTGGTGCCTCCGAAAGAAATGTAAAATTCGTGTGGGGGGGGAAAAAGGT  
TAJTTAGAAATTGTTGGCTTGTCTGTGCCGAAAGTATGTGTGGTTACGGGG  
AGTACGGAATTTCCAGGGGTGGGGGCGAGGCCGTGTGTCTTTAGCCCCG  
GGGTTTTTCCCGTCGCATGTTTAAGGGGGGGGAAGAGGGGGGATGTTTTCT  
TTCCGCGAAGGTTTTTGAAGAACGGCGTGG

>Contig36

CCCCCACCAGCCACTACTCAACCGGCCGTTACGAAACAACCTCGCCACAT  
CCACTAACCCGCTGGCTCACCACCCACCGCCCTCCCGATCCCCCAATCC  
AAACTCAACCCCAACCACCAAGCGCCTCCCCCTCCCCCACCCTCCAGCT  
CAGCCCCAACCTACCACCAACCCGACTCGCCCAACGAAACCAACAGCA  
AACCCAAATGCCACAAACCAAGTGTCCAAACCCCTCCTTCCCATCAGTTT  
GGTGGGCCCCTACCCGCTTCCCCCTGGCCCCAGGCTCTCCTTTTGTGCGCTT  
GGAGCAGCAGACTGATCTCCAGCCTTCACTCACTTCATGTGGTAATCTG  
TTGTGTTTCATCACTGTGAGAACTTCTGTCATCCCCCTCACTACTCTGCTGA  
AAACACTCTAGTGGTTCCTCATTTGCTCATTAAATGAAAGTCTAGATATTAA  
ACGTAGAAGGCCCAGCACAATTTGCCCTATGCCACCTACCTCTCTAATC  
TTTTCTCCTTACTCTGACAGACTCTCCGTCTGTCTATTTATGTATTCTTTT  
ATTGCTCTCTTCTACTTTTAGTATGAACTGGATTTATGGATTTTTTTAAC  
ATTGCTTTCAAGTATGGAATAAAGAAATTTTATTTATTTATTTATTTATTT  
ATTTGAGACTGGGTCTCACTCTGTGCCCCAGGCCAGAATGCAATGGTGCA  
GTCATATCTCACTGTAACTTCGAATTCCTAGGCTCAAGCCATCCTCCTGC  
CTCAGCCTCCTAAGTAGCTATGACTACGGGTGTGCATCACCACATCTGGC  
TAATGGAATAAAATATTACAATGCCATAATCTTAATTTTCAAAATTTTAAA  
TTACATTTGTACCTAATGCCCATGCATTTACTTTTTTTCAGTGGGTCAATAG  
CCCTCACTTTGGCAAAGGTCCCAGGCCCAAGGTAAGGCCTTACTTTTTTCC  
AAACTCATCTTTGAAAGACATAAGTGCCTGTAAAGTTGTACCACATTAGG  
TTCTAGGAATTTTTCATCAAAGACTTTATCAGACTATTTTCTCTAAGTT  
GAGAAAGAGCTGGGGGCGAGATATGGCACTGAATGACTGAAGAGAAGGCA  
CTGAAATCAGGCCAGAGGTTGCTGGAAAGAGCAATGAGGAACACCAGCAG  
CAATGAGGAGCCGGTGATGATTTTGGCTTTCACAGGGAGGTGTGTACCACA  
CCGATTTTATCTCTACGTGGATGAACCAAGCTGTGCGCTCCCTTGTCTC  
CAGGACATCACACTCTCCACATTCCCTCCCATCTTCCGGCTTCTGCTTCC  
CGGGGCCCTCATCTGCCCCATCCTGGGTGAACACTGGTCTGGTCAACTGCT  
GGGCGTACCTTCCCGCTCTGCACACCCTCCCTGGCCACCCCACTCTCT  
CACGGCTCGCACTGCAGAGGAGCCGCATCTCTAGCTCCAGCCCATCTGCC  
TCTTCTGAGCTCTAACTTCATGTAGGCGACTCCTGCCGGTGTGCTTCC  
AGGCCCATCACTTCAAAGCATTTTCCCTCAGAACACCATGTCTCTGGC  
TGCTCCCTCCAGAAGATACATCTCTCAAGCACATCCCCGCGGCTCTCACC  
TGGATGACTGCATTCACTTCTCCACATTTGCCCCCTCCTTTGGATGTA  
TATAGATTGTTTTAAATACAAATCTGATGTGCTTGTCTCTCTGCTTGAA  
ACACCTCAAACTGCCCTCAGGATAAACCACTGCCCTTGACATGTTTACA  
GGTTGCCCATGGCCTGGCCCTGCCCATCTCTTTCAGCCTCATCTCATGCC  
CTTGCCCCCTCGCTCTGCGGCTTCTGCCCTCCCTAGCCCTCCTTTAGGTTT  
CTAACACACCATAGTCTCTTAGTGTGGGGCTCTGCAAGTGCTGTTT  
CCATTGCCTGAGACATGAATCCCTCTCCCTATCTCTACCTGCACCTTCAT  
CTGATTAATCCCTACCCTTCTACTCATGATGTTGCTTCTCAGGGACTC  
TCTCTGACTTTTTAACTAATCAGGGTCTCCCCAGTATATATCTTCATAG  
CACTCTGTATTACTCCTTTCTTAATGACCACCTGCTGTAGACAGAATGTT  
TGTCTTCTCCAAAATCATATGTAAAACCTTCCACCAGAGCGATGATTAG  
AGAAGCCTCCC

>Contig37

GACTGACATTCAGAAGATATTAATAAGAGCACTAATGATGGGGATTGCAA  
CCATGTCTTTACTGACTTCCAGAAGCTTCTTACAGTAAACATGAAATCAC  
ATAATTTTCCACTTTCCTACTGTTTCTTGTCTGGGCTCTGTCTGCT  
TACTGTCTAATATCTTGGCCCCCTTAAAAGTTGCTAATCTTCAAACCTCA

FIG. 4 (14 of 61)

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TTCTGTGACTGGGCCCTGGTCCTTG...CATGGGCCTTGAAGATAC1CA  
CTGTACACTTATCTGGAGCATCCAGTGCCTACCACCTGACCCAGATTCTCT  
CATTGCGCTCCTCCCTCCTCCACCTAATGGGATTTGCTCATACCCGTGTG  
GGACCCCTCCCATTTCCTCCCAACTGAATACTTATCAAGACAACGCATTGC  
CATACTCCCTCGTACCCTGCTCTGGGCATCAGACTGAATGTTTGTTCCTCA  
TTGAGGATCTGCAGCTGCATCAGTTTCCCCAGCACCGTCCAACCCCTTGA  
GCATGGCTAGTCTAAAGCAGAGAATTAGCCTTTCTATCCCTGCTGCTAT  
ACATGCTGGGACAAATAATAAGAAATGACAGCATTATGATAATGCAGG  
CTGCAGGAGGCAGGAGGCAGGAATCAAATTCGTGCTTATCAAATAGTGCT  
CCAATTCTTTGAATATTGGACTATAGAATATGTCATGGATCTATGCTCAG  
GTGGGTTCCTATTACTCACTCCACTGAGGCCAGGTTGTGGGATTAGCTG  
TCCAAGAGGGGATTTTCAGTCTCACAGCATAGGGTCATTCTGAGAATTACT  
GGCCACACTTGTGTGGAGACCTCCAGAGAACAGAATCTGGGTGGTGCC  
ATGTACTTCCAGGAGGAGAGAAGTGGCAGGATGCCAGCCCCACAATCAG  
AGGGGAAGGGGCAGAGCCACATGTATGAAGATCCTCTCCCCAGTACGTGC  
CAATCACAGGGCTTCCTAGCTTTTGGGCCAAGGAAACAATGTGGGAAGCA  
AAAAAGGACAATTTCTCCTCCCTTTGCATGAAGACTGAGCAGTTTACC  
AGATTCCCAGGGAACACCTTCCACTCTGGGTTGAATGTGAGTGAGAGA  
CATTGAGCTGGAACACTAGAAAACTATTTCTGAGCCACTCACCTTTAG  
CCCTAGAAAGTGTGGATTTGTCTTCATCTTTGCCACAGTAGAGACTGC  
TGATAGCATCAGAACTGGGCTCTGGAATTAGACAGATATGGGTACAAAT  
CTGAGCTCTCTCACTTATTAGTGTGGGATGTAGAGCAACTTTAAATCC  
TTCCAAACCTCAGACTTCTCATGCATGATGTGAGGATTGTAATAGGGCCC  
ACCTAATAGGGGTTTTTGAAGATTAAAAAAGTTATTCAATGAACAGCATT  
TAGCAAGATGGCTGACCATTTGAGAAAAATAACAAATTGTTTATTATTATG  
TTATTATTAAACATCTTTCTGCACCTTCTGACTGGGGGCATCGTATCAT  
CAGAAATACTTAGGATGGGATGGATTCTGCTGAGGGCTGAGTCAAGGGTG  
CAATAATGGAGGAGTGAAGAAGGAAGAAATGGAGGCAGAAATCCCCAGGA  
GCCCAGCATGGTACAAGGCTGAGCTAGTGTGCTGCAGAGCCTCCTTGGACA  
GCCACAGAGCTTGCTCTGGCCCTGGAGGAACCTCTTCTAGCTGGCAGGA  
CCAGCCACAACAGTGGCCAGGGGATTTCCAGGGCGTGGGCTCCTCAGGA  
GTTCAATTGGACCAAGCCTGCCTGGAGAGGGGTTATAACAGGGATCCTTC  
CCTACTGGCAGGTGATTTACCCCTCGGTGAGAAGCTCAGGCATTTGTTTG  
ATGGAAGGTGGAAGGCCCTGTGCTGGGCCAGTACTATCAGGGATGGGCG  
GGTGGCTGGAAAATAGCAAATAAGACAATATGATAACACAGTTAACCACC  
ACACTATGTGAAGCTACAATATGGGTATCTGTAATAGACAATCCAATGT  
AGAGAATAATTTAAGGTGTCACTTCTCCCCGCCAATGCCATAAGCACAG  
GCCTCTGCCTGGGTTTCTCACTGTGGAATGTCTCTGGTCTCCTCATGC  
CCAGAGAGTGGGAAGTACTCTACTTTAACACCGGCTTTCTGTCAATTC  
CNTGCAGCCCTCCTCAGCCCCCTCTGCACAGGGAGGTTTCTCCTGCTG  
CTGCAGTGCTTTGTACTTGTAGTGGTACCTGCACACAGGTATTGGTGTG  
CTTGTCTCACCACCCTACATCACTGTAAGCTCCCCAGGAGCAGGCTTCCT  
GTTTGACTCACCTGTGATCCTCCACCTCCCACCCTGTAGTGCCTCAAGCA  
TTCTGTAGAGCACATGGACGCC

>Contig38

GACTAATAAGTACTTCATTATTTGGGTATTTTCCAAGAACACATATTGT  
AGGAAACCATTCTTTCTAAAAAAGTGTCTTTTAAAAAGGTGAATA  
ATTTTTGTCTAATTCAAAGTTTATTGAAAAGTTATGTATAAAACAAGGTA  
AAAGGAACAAGGAAATAAGGGAAATGTAAAGAAAATTATAGAAATAAAGT  
GGTATTTTTTGGTAAGAAAGCTTAAAGAGAAATAATTTTAGGTAAGAAAG  
AATCTTACCTAAAAATTTTGTGCTAGAATAAAGTGAAGTGGCTAAGAAAGGG  
ATGTTCAAAGCTATTTATGACAAACCCACAGCCAATATCATACTGAATGG  
GCAAAAGCTGGAAACATTCCCTTTGAGAACTGGCACAAGACAAGGATGTC  
CTCTCTCACCCTCCTATTCAACATAGTATCGGAAGTTCTGGCCAGGGCA  
ATCAAGCAAGAGAAAGAAATAAAGGGTATTCAAATAGGAAGAGAGGAAGT  
CAAATTTTCTCCGTTTGCAGATGCATGATTGCATATTTAGAAAACCCCAT  
CATTTAGCCCCAAAACCTCCTTAAGCTGATAAGCAACTTCAGCAAAGTCT  
CAGGATACAAAATCAATGTGCAAAATCACAGGCATTCTATACACCAAT  
AATAGACTAACAGAGAGCCAAATCATGAGTGAAGTCCCATTCACAATTGC  
TACAAAGAGAATAAAATACCTGGGAATACAACCTACAATGGACATGAAAG

FIG. 4 (15 of 61)

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ACCTTTTCAGGGTGAAC...GCAAACCAC...CTCAAGGAAATAAGAGAGG...A  
ACAAACAAATGGAAAAACATTCCATGCTTATGGATAGGAAGAATCAATAT  
CGTGAAGTGGCCATACTGCCCAAGTAATTTATAGATTCAATGCTATCCC  
CATCAAGCTACCATTGACTTTCTTCACAGAATTAGAAAAACTAATAGCC  
AAGACAATCCTAAGCAAAAAGAACAAAGCTGGAGGCATTCTGCTACCTGA  
CTTCAAACATACTACAAGGCTGCAGTAACCAAAACAGCATGGTACTGGT  
ACCAAAACAGATATATAGACCAAAAGAACAGAACAGAGGCCTCAGATATA  
ACACCACACATCTACAACCATCTGATCTTTGACAAACCTAACAAAAATAA  
GCAATGGGGAAAAATAATTCCCTATTTAATAAATGATGTTGGGAAAACTGG  
TTAGCCATATGCTGAAAACCTGAAACTGGACCCCTTCTTACAACCTTATAC  
AAAAATCAACTCAAGATGGATTAAAGATTAAACATGGCTGGGCATGGTG  
GCTCAGCCTGTAAATCCCAGCACTTTGGGAGGCCGAGATGGGTGGATCAT  
GAGGTGAGGAGATGGAGACCATCTGACTAACACAGTGAAACCCCTGTCTC  
TACTAAAAAATACAAAAAATTAGCTGGGCATGGTGGTGGGCGCCTGTAAAT  
CCCAGCTACTTGGGAAGCTAAGGCAGGAGAATGGTGTGAACCCAGGAAGT  
GGAGGTTGCAGTGAGCCAAGATCACGCCACTGCACTCTAGCCTGGGCAAC  
AGAGTGAGACTCCATCTCAATAAATAAATAAATATGGAACCTCTCCCAACA  
CAATAATAAGACAAACCCCAATGTTTTAAATGGGCAAAAAATATTGAA  
CAGACACTTCACAAAAGAGGATATGTAAATGGTCAAAAAGCACATGAAAA  
GATGTTCAACACCATTGGTTCATCAGGGCAAAGAAAAGTAGAACCAATG  
AGATGCCTCTGTACACCACTTAAATGTCCAAATTAAAGAAAAAAGTTTT  
GGCAAGTTGTGGAGCAACTGAAATGCTCGTGTATTGCTGGTAGAAAAAC  
AAAAATGGCATAACCATCGCAGATAATTTGTTGTGCTTTCTTACAAAGTT  
AAACATATACTTATTGATATGACAGTTCATTCCAAGAGAAATGAAAAACA  
TAAGTCCACACAAAGACTTGTACCTGGGTGTTTATGGTAGCTCTATTCTAT  
AATTGCCAAAAATCTGGAAACAAATCAAATGTCCATCAGCAATGGAATGGA  
TATACAAATTGTGGTACACATGTACAATAGAAAAGTACTCTGCAATGGAG  
AGAAATTAACCATTGACAAACACAAAAACATGGACAAACCTCAAAAAACAT  
TATGCTGAGCAAAAGAGCCAGACACAAAGACTGCTCAGCGCATGATTC  
CATTCATATGAAATCACAGAAAGGGTCAGTTGAAGGTGCAGAGACAAAAA  
GTAGATCTGCAGTTGCCTGGGGATGGGGTGGGAGGTTGACTGCTCTGACG  
CGTAAGGAAATTTGGGGGTAGGTGGGGGATGGTGGGAATATTTTTTGAAT  
TGAATTGGGTAATAGTTTTTAATAGGTAAATATTGGACCCACAGTATTT  
GAGATAGGTTTCAGTCAATTTAGACAGTTTATTTTGCCAAGGTTAAGGAT  
GCATCCGTGACCCAGCCTCAGGAGGTCTGACAACCTGTGCTGAAGGCAG  
TCAACATACAGCTTGCTTTTATTCTATTAGGGAGACATAATACATCAAT  
CAATGCATGTAAGGTTTACATTGGTTCAATCTGGAAAGGTGAGGGAACTT  
GAAGCAGGGAGCTTCCAGGTTACAAGGTAGATTATTCTCAACAGAAAGGA  
ATGCTCTGGTTATGATAAGCGGTTGTGGAGACCAAGGTTTATCTTGTAG  
ATGAAGCCTCCGGGTAGCAAGCTTCAGAGGGAATAGATTGTCAAAGTTTC  
CTATCAGACATAAGGTCTGTGTTGATGTTAATGCTGGTCAGCTTTTCCTG  
AATTCCAAAAGGGAGAGGGGTATACTGGGGCATGTCCAACCTTCCCTTCC  
ATCATGACCTGAACTAGTTTTTTTTCAGGTTAACTTTGGAATGCTCTTGGCC  
AAGAAGAGGGGTCCATTGAGATGGTTGGGGGGGCTTAGAATTTTATTTTT  
GGTTTACAGTGAAGACTTTTCAAGCTAGACACTTAAATGAGTATGTTGCA  
AAATGGCAATTTCTTAGCACGGC

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GACGTCCTAAAGAAATGCTAAGGTAACCTCAATTAACCTATGCTAGAAAAGA  
GAGTTAAGTATTTAGGAGGATTTAATATGGTGTAAAGTTGTGAAAATCA  
AAATGGAGACACTAATGTTAAGAAAACCTGATAAATGGAGCCAGGGAAG  
GCCATGAAGAAAGAGTTCTCACACTTGATCCCTGATCATGAAAAAGACT  
CTGCAAAAAACAAAAACCTTGACAAAGGCCATTGCAACCTTACACAAAAA  
ATACTACTTTAAAAGGACATGTGCCCAGCAACTGCCTGTCCAACCTCAGA  
CTGGCAATATCTTTGTTATTGATCTTAGTAGCCAGCATAACTATTTCAA  
AACAGTGATGTAATGCTCATTTTTTTTTCTTTGAAAACCTTTGTCTTCCT  
GTAAAAACCTTTGTCTTCTTTACTTACCCTGAATATGCACAGAGTTTACT  
ATGGAGTGCATATTCCTGTTGCAATGCTCTATTCCCAACAAACATCATT  
TTCTTTTAGAGAGCCTCTCTCTGTTTGTGATTTAGGTTGGTGATGTAAAG  
CAATGGCATAACTGAACACTGATTCAAAGAAAAGTGGCTTTTCTCTTGT  
TGTATTAAAAAGAGGCCTTATAAATAGGATAGTAAGATTTGTAAGTTGAA

FIG. 4 (16 of 61)

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CTTAAAGCATGAAGAAAATTTAGGGGCCAGGCAGGGTGGCTCACACCTGT  
AATCCCAGCACTTTGGGAGGCCAAGACAGGAGGATTGCTTGAGCCAGGA  
GTTCAAGACCAGTCTGGTCAACACAGACCTCATCTTTACTAAAAATAAAA  
AAATTAGGCCAGGTGCAGTGGCTCATGCCTGTAATCCAGCACTTTGGGA  
GGCCAAGGCGGGAGGATCACTTGAGGTCAGGAGTTCGTGACCAGCCTGGT  
CAACACGATGAAAACCCCATCTCTACTAAAAATACAAAAAATTAGCTGGG  
TGTGGTGGCGGGCACCTGCAATCCAGCTACTCGGGAGGCTTCAGGCAGG  
GGAATCACTTGAACCTGGGAGGCGGACATTGCAGTGAGCTGAGATAGTCC  
CACTGCACCTCCAGCCTGGGCGACTCAGCAAGACTCTGCCTCAAAAAA  
AAAAAAATTAGTCAGGTGTGGTAGCACACAGCTGTGGTCCAGCTACTC  
GGGAGGCTGAGGTGGGAGGATCATCTGAGCCAGGAGGTCAAGGCTGCGG  
TAAGAGCTGAGATTGTACTACTGCATTCCAGCAGGGGCTACAAAGTGAGA  
CCCTGTCTCAAAAAAGAAAAAGAAAAAGAAATTATGTTTTTAAATTTA  
TAATTATAATAAATTTAATTACATAAATTTAAGCTCAAGTAATTGTAAAT  
ATTCTTTCTGTGCACATAAGTTATTCTTGTATTGACCCACAGGAGCTGG  
CCATTCTTCAAGTCAGAAGGCCTGAGAGAGGAGCTGCCAGGTGGTCTTC  
ATGGGGCTGTGGGCCAGTCATCCCCACAGGTTGACAATCCTTGTGTAC  
TTCATCCTCGTTGGATCCTCTGTATCCCTGACGATGAGCAACTGTGAGGC  
CCGTTTCAGCACTGAGTTCAGTCAGGAAAAATCCACCCACCCACCACA  
CGCTCACACTTACACACACATTACACATGCACACAGTTCCTGGCTCCGA  
AAAAGAAAAAAGCAATTTAAATAATTCTGATCCTTTGCTTATTT  
CCACAACTCCATGAAAATTGTACATTGTCCAAGCAACATTTCTTAATAT  
TCTCTTTTCTCTCATATCCATTTTCTTACTGCTGTCTCCACCTTTCTC  
TTCCAACTCCCTGTAAATCCCTGCCCCAGCGAATTTTATTCAATTT  
TGTGGAATGGAGGCTGCTGTGATTAAATTAATAAAAAAAAAAAAAATCCC  
TACTCCATGTCCAGATCCCTAGTTGTTTTTTGTTTTTTGTTTTCTGAG  
ACAGGGTCTTGTGTCTTCCATGCTGGAGTGCACTGGCATGATCATGGCTC  
ACTGCAGCCTCAACCTCCTGGGCTCAAGTAAATCTCTTGGCTCAGCCCTC  
CCCAGTAGCTGGGAGTTCAGGTATGTGCTACCATGCCTAGCTAATTTTT  
TCTTTTATTTTGTAGAGACACGGTCTTGCCAGGTTGCCAGGCTGGTATA  
GAACCCCTGGGCTTAAAGTGATCCTCCTGCTCGGCTTCCCAAAGTGCTGG  
GATTACAAGTGTGAGGCACTGCACCCAGGCTGGATCCCTGCATTTTACA  
GATTTAGCATCACAAAGTCTAAACAATTAGACTGACTAAGGCAGAACTG  
CCCTTATGACAGCAGACATAAGAAGGAAAAGGCCAAAAACACTGTGTAA  
AATTATCCAAATGTGAGGAAAAGGCCAAAGAGAGTAGGTGTGCCTTTTAG  
TGTCTAAGCTGCCTGCCAAGGGGCATCTGATGCTCTCAGGCAGGAGTCC  
ACAAATTTTTTTTGTAAAAGATCAGATAGTAAATCTTTTCAGCGTGAAG  
AGCATGAGGTCTCTGTCAAAATACTCAACCACCATTAACATGAAAGC  
AGCCACAGACAACACATGACAAATGAGTGTGGCTGTGTCCAGTAAATC  
TTGATTACAAAAACAGGCAAGAGGCCAGAGCTGACCCATGGGCCATAGTT  
TGCTGACCCCTTCTGTAAAGGAAAGTATTTTGTGTTGACTTGCTGTTTAC  
CATTGATTGAACACAAGGCTCTGTAGAGTTACTTGTAACTTGAGAAGA  
TTGATGAGTGGCAAGTAATTTTTATTCCAGGAATATANNATTATTCTGT  
TCAGTAGATAAGATAAAACCCACTGTTATATTACTGTCTTGTGTTAGAAATG  
GACTTTGATTCAATTTTTTACAAATTCATATTATTGCCCTAATTTGTATA  
TAAGTATGCTTCTTTTAAAAATATATATTTTTTAATAAATTTGAGACAGG  
GTCTCACTAGGTTGCCAGCCTTTTGTATAATGAGAGCATAAAGTGAAT  
TTCACACTTTAGCCTAGTGATAGATGGGATTACAGGCACAAACCACTGC  
ATGCAGCTAATTTGCTTCTCATTCCAGCAGGTTCTATTCCNNNGNTTTT  
CATATACGCGTCTCTTAATGC  
>Cont1940  
CGCATTTCAGCCCAAGTTTTCTTCAGTGTTAAGGTTTTTGTACTCTGTGC  
CCAAATGTCTTCCAAAAGGTTAAGTTTTTTTACCTTCTGCCAACATT  
ATATGAAAGTGTCCACTTTTGTAGACTTTTACCAATGCTGACTACTTTG  
GTTTCAAAAAAGCTCTCAGTAATTTTCTATTAAATTACTTTTACCTTTT  
TATTGAGGGTGTTCACCTTTTATTGTTAGCATATTCTCTCTGGGCTCCA  
TTGGACSCCTTGGCAGCTTTTTGGTAGTAGGTGCCTTTAGAAAAGTCCTT  
CTCGTCTGGCCCTTTCTGAGCAAATCTAGTGAACAGAATTGGCTCCATGC  
TCAGCATTGCTTAATACGGTTGATCCAGGGCCTAGGACTCATTCTTCAT  
TACCATCCACTTGCATTGTCTTAAAGCAAGGCTCTATTAATTTAATTTGG

FIG. 4 (17 of 61)

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CATTTCTGTGCCAGCTCTTAGTTCATTAAACAAAGGCTTTAGAAAA  
TCCCAGTAGATGCCTATGTTGCTTCCTTTTAAAAAATTTTGGAGCTGTTT  
CCCTAGCCTAACCTTTTCTCAGGGCAGGAGTTAAGTCCCTTCTACTGCA  
TTCTGTGAAGATGGTGAATCAAGAGGCAGGGCACCTGTTGCTTTGTGAA  
ACAGTCCACTCTGCAGCTGGGCAGCTCTGTTACTAGAAATGTTCTCCCTTC  
TGGGGAGCCAATATTTTGATGTCCTCTGTGAATCTCATCTGCTTATCCCA  
TCTGTTTATGTCCTTGAAGATGCACAGGTCTGACACCACGAGGTAGCCCT  
TAGAAATTTGATGGCATTCTGATGTGTCCCCAACTCTTCTCCAACCACT  
CCTCCCAGAGCTTGTCTTAAGCCCTTGTGGAGCTGATTGCTTTCCCTC  
AAGGCAGCTCAGTTTTTCCCAGTTTGCTCCTGGTGGTCTGAAATATGAT  
TGACTCCTGAATACTCCAGGTGTGAAGGAGAGTGGGGTGGCTTTCTAC  
TTGTGATGGCCTGGGTTTTAAGTTGCTGTCCAGTGGAGCAGAGGTGACTT  
TCCCAGTGAACATACATTTTTCCCCTCTAAATCCTTAGCAATTTTGTCTC  
CAGAGGCAAGACCTGGCCAAACCATTTGTGTTGAGGATTGAATCAAGAAT  
GATTGAGGAGATGACAGTAGTCCCCCTCATCTGAGGAGGGCGTGTCCA  
AGCCCCCTCAGTGAATTTTCTTAAGCCCTTGTGGAGCTGATTGCTTTCCCTC  
CTATGATTTTCTATAAATTAATACATGCCTGTGACAATGTTTAATTTAT  
AAATTAGGCAAAGAGGCCAGGCGCAGTGGCTCAAGCCTGTAATCCAGCA  
CTTTAGGAGGCTGAGGCCTCACCTGAGGTGAGGAGTTCGAGACCAGCCTG  
ACCAACATGGAGAAACCCCGCCTCTACTAAAAATACAAAATTAGCTGGGC  
ATGGTGGCAGGCGCTGTAATCCAGCTACTCGGGAGGCTGAGGCAGGAG  
AATCACTTGAACCCGGGAGGCGGGATTTGCGGTGAGCTGAGATCGTCTCA  
TTGCCACTCAGCCTGGGCAACAAGAGTGAACTCCGACTCAAAAAAAAAA  
AAAAAATTAGGCAAAGAAAGAAATTAACAACAATAAGTAATGAAATAGA  
ACAATTCTAACAATATACTATAATAAAAGTTGTATGAATGTGGTCTCTTT  
CTCAAAATTACCTTTTTTTTTTGTAGACAGGGTCTCACTTTATTGCCCAGG  
CTGGAGTGCAGTGGCAGCATCACAGCTTACTGCTGCCTCGACCTCCTGGG  
ACCAAGTGATCCTCCCCTTTAGCCTCCTGAGTAGCTGGGACCACAGGCA  
TGCACCCTGTATCTGGATAATTTGTTTATTTTTTTTTTGCAGAGAGAGG  
AGGTCTCACTATGTTTCCCAGGCTGGTTTTGAATGCCTGGGCCCAAGGGA  
TCCTCCTGCCTTGGCCTCCCAAAGTATTGGGATTACAAGCGTGAGCCACC  
ATGCCTGCCCCAAATTTATCTTATTGTTCTATACCACTCTTCTTCTTGT  
GATGATGTGAGGTGATCCATTGCCTCCTTGATGAGATGAAGTGAGGTGAC  
TGATGTGGGCATAGTGATGCAGTGTTAGGCTGATATTGGCCTGATGATA  
TGTGAGAAGGAGGTCACTGCTTCCGTGATCCTGGATCATAGAGTCATG  
ATGATGTCAATGGTTGGATGTGAGGAGCAGACGATGTCAATGACTAACGA  
TAAGCTGGACAGGTGGGATGGTGGCACAAGATTTTATCAGCCTACTCAGA  
ATGGAGCACAATTTAAACCTTCTGAATTGTTTATTTTTTGGAAATTTTTCAT  
TAATATTTTTTGGATTGCAGTTGACTGTGGGTAAGTGAACCTGTGGAATGT  
GAGACTGTGAAAAGTGAGGGAGTACTGTATTATGGAACCTGTAACCTCTAT  
TCGGTAGGGGAACAGAAATTCATTTCTCGTTGTAGCAAAAATTTGGCTTTGGA  
ATCAGACAGATTGATGTTTGTCTATCATTTCTAAATGGGTGCAGCTACACTT  
TCCTCAAGAGGTAGTTCTGAAAATTTAACAAAATGTGAATTTCTTGGTAA  
AAAAAAAAAACCTCAAAAATATTCAGTTTCTTTCTTTTGTGTCTGATGT  
ACTCCATCAAATACTGGGAAATATGTGTCTCTCATAGAAATGTGATGGAT  
CTTTGTAATCTGATTATCCACAAACCTTGGGGATTAGCTGTTTCAATGT  
TCCTATTTTACAGATAAGAAAATGGAGCCTGTGGTAAGTTAAGTGAGTTA  
CTCATGGCTACTTAACATAATTTTACTAGGTGATAGGCCAGAGCTAGAG  
CCCAGGTACCTTCTTATCAATGCTCTGCCTTGTCTCTGTGCCTTCTGT  
CTGTCTGTATGTGTATGTGCTTGTGACAGTAAGGCATAGTTTAAACCCAG  
TAGAACTACCGGTTTGTAAATGAATCCACTTGTAAATGACTGACCATTCA  
AGGAACAAGTGTTTTTCTATGCTTGACACCTGTTTGGATGCCAAAAAG  
GATACAAATGTAACCTCAGACACTCTGGGCCTCATTTTGCACTCATTAGC  
ATGTCCAAAATTAAGAAAGACTGACCACCAAATATTGGTGAGGATGTGG  
AAGAACGGGAACCTTTCATACACTGCTGGTGGGGATGTAAATGGTACAAT  
CCCTTTGGGTAAACAGTTTGACAGTTTCTTAAAAAGTTAGACATATATATT  
TACCATATGACTCAGCCCTTCCACTTCTAGGTCTTTACCCAAGAGAAATG  
AAATGCTGTGCTTTTACAAATGTCTATACAGGAATGTACATAGCAACCTT  
ATTTGTCAATTGCAAAAAACAGAGACAATTCACGTTGTCAAGAGTGAATG

FIG. 4 (18 of 61)

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GATGAGCAAGCTGTGGT...GTCTATGCA...GGTATCCTACTCAGCCAG  
AAAGATATGGCTAAT

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GACAACAATGTCATGCATAAGATGACGATGGCCTGGGTGATTGATGCAAA  
CAAGGATAAAGAAAAATAATCAATTTTGTCCCATTTTCAAAGACAGATAG  
CAGCAGCAAGAGTGTAAAGTCTGAGGAAAGTCATATTCCTTCCTCTACAA  
CATAGCACACACACTTACAAAAACAATACACAGACTCCTGGCCAATGGAC  
TTCAAAACTGAGGAGGATCATTAATTTAAATGTTTACCCGCTGCATGAAA  
TCTCCCTGGGTCTGCCCTCCCTTCCCCACCCTCCTCCACTTGGGCCGGG  
GCACAGCAGTGATTCTCTCACCTCTCAGAGTGAGCCAGTGTTGGCTGCAT  
TGAAGGCTCCAGATATGCAACAGGGCAGATATTCCTGGACCAGGGTGCA  
CAGAGTGAGGCTCCAACGCACCCTATTAAGTGCATGAAGGATGAATGAGC  
CTCTGGTATGGGCTGGGACAGAAAAAGGATTCAAGGGGGCCAAAAGGGT  
TTGGGTGGAACCTACCAGGAGCGGCAGTACAGACTCCTTGGGAAGGTGGC  
CATGATTTAGCCACATTACCAATAGGATAATCTGGAGAATTTCTAGCT  
TGAGTTTCTGGGAGAAAGCAGATTTCTGGATTATCTGGTGACAGGTAACA  
GGGCCGAGTTTATCCACAGCCACCTGCAGTGTTAGCACCTTAAGCTGAGT  
TCCTTGACCCAGGATGCTGTACGCCCCAGTCAGTGAGACGGTTCTTG  
CTGAAGGACTGAAAAGCTTGGGTAAGTGACTTCACCTAAGCCTCTATCTC  
TTGCTCCCGTAAGTCAGGGCTCATTGTGGCTCCTTGCAGGCTTGACTTCA  
GGGTAAACAGAGAAAAATGAAGGTACAAGTGCCTTGTGAACCTCTGAACCTC  
CAAACCAAGTCATTCTCAAAGTGCCGTCCACCAGTCTAGCACATCAGCATC  
ACTGGAAGCTTGTGTTGAAATGTAAATTATCAGGTCTCCAGAGCTATGTA  
TGAATTAGAACTCTGGGAATGGGGCCCTGCAATCTATTTCAACAGGTCC  
TCCAGGTGATTCTGATGCAAGTTAAAGCCTGAGAACTCTGTCTTATACA  
AATGGATGTCAACTCAAGCTGCTCTTCAGAATCACCTATAGCACTTGTTT  
ACCCGAATCCCTGAGAAATGGAGCTTCAGGACTGCTATTTCTCAAAGTTTG  
CCTGGTGATCCTGAGATGGGGTTTGGGGGACAGAGATCCAAGGTGCTACC  
AGGTGTGAGGAATTGTTAGAAGGCAAACCTGGCTGTCTATAGGGTGCTT  
AAAGGGTACAGATCCTAGGATTCTGCCTCTTACAGCTGAATCAGACTTTC  
CTAGAATGGGATTGCTGTCCAATGGCATGCCTCCTGGGTGACTCTGATGT  
ATAGCCTGGGCTGGGAACCAAGAGGATTATCTTCCATTGACCAAGCTG  
ACAACTCGCTTAAGGCTCTGAGTTTCACTTTGATTTTCTAGCCCCTGT  
CCTTCCATGGATCACCTGCCCCCTTCCCTCCTAATCAGGAGCACAGTCAG  
TGGATGCACTAATGTGGCCTCTCCTTGGCTGCAGGGAACAGGTGGAAATG  
TGGCCATAGGTGTGTCAGGGCTGCCCTGCCATGTATTAATAGCTACAGATT  
GAAAGATCCAAGGACAAGAGACTAGAAAAAAATTTAAACAGCCAAGCAT  
TGGCCCAGTAATGGCATTTCAGAAATCCACCAAAATATTAAGATGCTTTT  
TGAAAAATATCCAGAGCACTCATGTAAAGTGCTTAATTATTAATAAAG  
CTGACATGTGTTGGGTACTTCTGTGGGTCTGGCACTAGGCTAATTATGT  
TTTTAGGAGTTGACTCAAATGCTCCCTGTCTAATTTATGTGAAAAATAT  
AATTATTAGCTCCATGGTACAAATTAAGGAGAGGTTACATAAATAAAG  
GAATGATACTCAAATTAGTAACCAAGAGCCCATGCTCTTAAACACTATGCT  
ATTATTTGTGGACTCTTACATAGGTGGCAAAAGTCAAAGGCTAGATTGAC  
TTCTGTCCACTTCCAGCCAAGATGAAGTACAAGATTGAGATACACCCTTC  
CGCATTAACAACCTTAGGAATCAGACAAAATATACAAAGCATTGTTTGT  
ACACATTGGATAACAGACAGCACTAGATAGTCGTGTCTGAGAAAAGCGGT  
GAAATGAGCTGAGTCTTAGAATTGCCCCAGTTTACTAAGGGGCATAGTAA  
GGGCATAGCTGCAGCACAAAGAAGCAGAACCACAGAGACTGGCGTTCA  
CCTGAGTTGAGAAAACCAAGTTGAAAATTTAGGAACACTAACACAGATAT  
GTAGGCAAGAGTATCAGAGAGGAGACAGTTGTAGGGAAAAAGAGAGCTTT  
ACAGAGAGACAGCGAGAGCTCCAGAGACCCGAGAAGATTGCCCTGACGT  
CACTAGCTGAGTACCGATCAGTGATACATGTAAGGATATTACTCAATAT  
GTGGAAGAAGACAGAAGGAATGATGTCAAAGCTCACCCAAAGACAGGAA  
TCATTTATGTTTCCACCAGCCAGAGTGGAACAACCTTGTAAACGCATATGG  
AGTACTCAAACGAATATTTCTCAATAATAAGTTCAAATTAAGTGAAGT  
AAAGCCTGCCCCGCTTTGTCTGGACATGCCTAACAAAGCTTTGAGGGAAGC  
CTCAAAAGAATGAAACCGTGTCCAAGTAATTTAACTGTGTCCAGAAAA  
AATTCAAGAACATTTAAATAAATATTTAAATATGATCAAACCCAGCAAGG  
TTAAATTCAAAATGTCTGGCATCCATTAAAAAATTACCAGCCTTGAAAAAT

FIG. 4 (19 of 61)

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TGGCGGGGAAATATTA: :ATAATGAA :AAAAAGCAATCAACAGAT  
AGGCCTAGAAAGTATACATATGATAAAATTAGCAGACATTAAATGGTTAT  
GATTAATTTATTTTATATGTTAAAGAAGGTAGAGAAGAGCATAAGCACAT  
TAAAGAGAGACAGGAAAGTCCCAGTACTCACACAGGGCCAGGAGCAGTTT  
TCACCAAGTCAGGTGGGAAAACCTTCATTTTCATGGAGCATTGGTAGAGTA  
CACAGTGTCTTGCCTTAGTAGAGGGATAAATGCTGTTCTGTTCCCGCCTA  
ACCCATCTTGAAAGAAAATCTGAAAGGATCAAACCTGTATTCAAGTAACCT  
AATCACATCCCAGCACACAGCTCGACTAGTTATAAAAAACAAAAATATTA  
ATATCTAGAAACACAAAAATAATATCTAGCACCCAAACAGGTAAAATTCA  
CAATGTCTAGCATTCAATTGAAATTTTCTAGGCCATCAAAGAAGCAGTAA  
AATATGACCTATAAGGCCGGGCACATTGGCTCATGCCTGTAATCCCAGCA  
CTCTGGGAGGCCAAGGTGGGTGGCTCACCCGGAGGTCAGGAGTTCAAGAC  
CAGCCTGGTCAACATGGTGAGACCTCATCTCTACTAAAAATATAAAAAATT  
AGCCCAGCATGGTGGTGGGCGCCTGTAATCCCAGCTACTCAGGAGGTTGA  
GGCAGGAGAATCGCTTGAACCTGGGAGAAGGAGACCGCAGTGAGCCAAGA  
TGGCACCAATGCACTGCAGCCTCATTAGAGAACATCGGGAAG  
>Contig42  
GAAACTAAAGGCTTATTTAAAGCGCGAGACCGTGGCGCCTTTGGACTGGA  
CCCTTTCTAATGATCATTTAGTATCAGGCTATGTGGGAGTTGACCGTTTT  
GCATAGCCTGAAAGCCAAACAGTATCACTCCTCCTTAGGTGTGGCAGAGA  
TGTGAGAGAAGGAGACTGACAGTCTGTGGGTGTGTATGCAGTGTGGGGG  
AAGCAGGCACAGGGGACAAATACTGTGGTGTAGAAAACAGTCTAAGGTA  
GCATCAGGAAATTCATGAAACC AAAATGAATTTCTAATACAGCACAAAGACA  
TTATTTGTTTTTGCCTCCCTCTCATTTTTTTTTTTTTTTTGAACAGAGTC  
TTGCTCTGTCTCATCCATGCTCGTGTGCAGTGGTGCAATCTCGGCTCACTGC  
AACCTCCACCTCCAGGGTTCAAGCAATTCATGCCTCAGCCTCCTGAGT  
AGCTGATTACAGGTCTGCACCACCCCGCCGGCTAGTTTTTGTATTTTTAG  
TAGAGATGGGGTTTTGTAATGTTGGCCAGGCTGCCCTGTCATTTTTTTTT  
TACTAGTGTCCAGTGGAGTTTTTTAGGGGCTACATAACATGATACTGTCA  
TTAATCTAATGGCTAATGAAAGGGATATGTATATGTTTTTGTGTTTAAAA  
CAAACCTTCTTTGGGGTCTCAATAATTTTTAAGAGTATAAAGGGTCTG  
AGATCAAAGAGTTTGAGTTCTGCTGGACTGGGACAGTGGTTGTCAACCCA  
GATTGTACATTAGGGTCATCTGGGAAGCTTTAAATAGTACTGATGCCCA  
ACCTTACCGCAAACCAATTAAGCCAGAATCTCTGTGGATGAGAAGTCTTC  
ATTGTCATCATCACCATGACCATCATCATTGTACCGTCACTACACCATT  
ATCATCATCATCATATCATCTTCATTATCATTGTTAGTATCTCCATCACC  
ATCATCAGCATCACCATTATTATCATCATCATCATCCCCACCATCATCCT  
CATCGGAACCTCACCTGCATGGAGGACAATCCACTATGCATTAGGTGCTA  
TGCTATTTGCTATACTCCTTATTCTCACAACCTGCCAGAGAGGCTGATAT  
TATCTCACTTTATAACAGGAGGAATCTGGATCGGAAAAGTTAAGGTAAGC  
TAATTCACAGAGCGAGAAGAGATAGAGCCAGGATTCGAAACAGTCTCT  
GCTACATCAATGTTCCAGTCTTGCCTTGCCTATTGAGAACCTCTTTAGTTAT  
GCTTTACCCCTCCAACACCACAGTAAATTTTTCTTTTTTTAAAAAAAT  
TATACTTTAAGTTATAGGGTATATGTGCATAATGTGCAGGTTTGTTACAT  
ATGTATACATGTCCATGTTGGTGTGCTGCACTCATTAACTCGTCATTTA  
CATTAGGTATATCTTCTAATGCTATCCCTGCGCTCTCCCCACCCATG  
ACAGGCCCTGGTGTGTGATGTTCCCCACCCTGTGTCCAAGTGTCTCATT  
GTTCAAGTCCCACCTATGAGTGAGAACATGTGGTGTGTTGGTTTTCTGTCC  
TTGTGATAGTTTGTCTCAGAATGATGGTTTCCAGCTTCATCCACGTCCCTA  
CAAAGGATATGAACTCATCTTTTTTATGGCTGCATAGTATCCATGGTG  
TATGTGTGCCACATTTTCTTAATCCAGTCTATCATTGCTGGACATTTGGG  
TTGGTTCCAAGTCTTTGCTATTGTGAATAGTGCCACAGTGAACATTCATG  
TGCAATGTGTCTTTATAGCAGCATGATTATAATCCTTTGGGTATATACCC  
AGTAATGGGATGGCTGGGTCAAATGGTATTTCTAGTTCTAGATCCTTGAG  
GAATTGCCACACTGTCTACCACAATGGTTGAATTAGTTTATAGCCCCACC  
AACAGTGTAAGAGCATTCTATTTCTCCACATCCTCTCCAGCAGCTGTTG  
TTTCGTGACTTTTTAGTGATTGCCATTCTAACTGGCACCACAGTAAATTT  
TTATAGATTTTATAAGCAAATTGTATTTACTGTGCAAGAATTGGTTTATT  
TTTTAAACCATGTGTTGCAACATACAATGGTTAATTGTGATTTTGCTC  
AGTACAAGATCATCAGATCACTACACAGACTTGAGGTAATTCACCTAAA

FIG. 4 (20 of 61)

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AGCAAAGAGAACTGACCCACATTAAGTGAAGAGTCTTTACTTATTTA  
CCCTATAAACGAGCCATATGAAGAGAAGGCCTTAATGTGGTTAACTATG  
TAATTTTTTTCTGACTTTTTGAAATACTGAGAAGAGCTCATGACTCTCC  
ATCTCCTAATTCTACCTGGTGGATTAGACTGACCACAACTCATGGGT  
AAATGAGGGAAGACGAATAAGAAACCTTGCTTTTTTCTCCTTGTTTT  
TGGCTGGCTGCAGTGGCTCACACCTGTAATCTCATCACTTTGGGAGGCCA  
AGGTGGGAAGATCACTTGAGCTCAGGATTTCAAACTGGCCTGGGCAACA  
TAGTGAGACCCCATCTCTAAAAAAGGCGACGG  
GCGGTGCGTGCCTGTAATCCTACCTACTCAAAAAGCCGAGGTGGAAGAT  
CACTTGAGCATGGGAGGTCAAAGCTGCAGTGAACCTTGATTGCACCACTT  
CATTCAGCCTGGGTGACAAAGCAGGACGCTGCCTCAAAAAACAAAAAC  
AAAACCTTAATTTTTTGGCTATTCTTTCTGGTAAGAATGGTATAGAGAT  
GGGGATGAGGATGGCTATTGTATGAGAGAGCAAACAGGGTCCAAGCAGTG  
CTCTGGGCTGTCTAAGGACCAGTAGTCAGCTTAACCTTCTCAAATTTCCAG  
GGAAGGAGTTGCGAGTGGTAGAATATCCTGGGTATGCCAAAGCATCACC  
TTGCAATAGCCTGTCTGAATAATTTGTTTCATTGTTATGACTGGAAA  
CTGGCTTTGTGTATGCCAGAGAATGGGGGCAGGAAAGAGAGATTGGTGTC  
TTGAGCTCTCTGTGCTCTGGGGCAGTGATGCTTTTCTCTCATGTGGAA  
GGAGAGCATGACTGAAAAGGTGCACAAATAAGGTGTCTGTGAGAGAAAT  
AACCTTCCAGATACAGAGACACAACCTTCCCCAAGAGGTCTCATTGCTC  
TGCCTTTTTCTTTTTTTGCTTGTTCTACCATTAAATAACAGAACTGA  
TTATGACCTCAAAAGAGAGGAGAAAGCGACTCTCCCCACCCTAGAGCTAG  
TTAACACCATACTCTCCTAGATCTCAGTTCAAGAGTCACTTCCATCCCC  
AATAAAAGCCCTTGAGTGCTGAGCACCTCTCGTCAATGCTTGTCTA  
GGGGTTTTGTACATTTTCTGTGTGAACTTGGGTGACATCTGTATTT  
CCGACTAGATTACAGTTTCTCAAGGGTAGGGATGTCTTGCTTGCCATTT  
TCAGTTCAGCATCTAGACAGTACCTCAAGCAAACAAGGCCGAGGGGGT  
GCGGATCAGGAGTTCAGGAGTTCAGAGACCAGCCTGATGAACATGGTGAAA  
CCCCGTCTCTACTAAAAATATAAAAAATTAGCCAGGCGTGGTGGCAGGTGC  
CTGTAATTCAGCTACTCAGGAGTCTGAGGTAGGAGAATCGCTTGAACCC  
GGGAGGTGGAGTTGAGTGACCTGAGATCCACTGCACTCCAGCTTGGGT  
GACAGAGCAAGACTTCGTCTCAAAAAAAGAAAGAGAAA  
AGAACATCAAATGAATGAATGAGTGAGATGAATGAGTTAGCAGTGTGGA  
TTTAAGTGTCAGATTCTTCCAGCTTGACTTTTTCTTTGGCTTAGTGAT  
TTTGAGGTGTCAGATTTATTTTCTTTTCAAAAGGTGATCACTACCATA  
AGATCTTCAGAAAAAGAAATGTGGCAAGCCANGTCTCACTAATGCAATCT  
CTATAACAACTGTATCAGTACT

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GAGGTGTCAATAATATGGACCGATAGATGAATACAGGTAGGATGGGACAC  
AATCTAAGATCCCAGGGGGGGGAGACCACACGCTTGTTAGGGAGACCCA  
AAGTGGACCGTGTGGCCAGAAGAGTCCCGCACTGCACTCTAGTGACAGTG  
CAGAAAGTCACTGTGGGAAATCTAGAAGTTTCTACAGGTGCTATTTTAT  
CATAGCACTGTGCAGGCCAACCTTCTGCTCCACTGGCTGTTGGGAAAA  
GCTTTCTTTTTCTTCTAGCCAGGGAGCTCTCAAAGTGTTCCACTCTCT  
CACCTCCACCCAGGCGTCCAGGTGTGGAGBACACTTGCCGGCTGCTTGTC  
TGCTGACTCATCCCTTGGTTTCACTTGAAAAACCTACCACCAGCTGGCCT  
CTTTCCAAGCATCAGCCTCCTCATTTTCTTAATCCCTTAGGTGTGATCTC  
ACCTCCACACAGTAGATTGCCTCAAGGCCCAATTCCAATATGAATAAAAA  
TGATTATTTTGTCTATCTTCCAATCTTCTTTTAAATATTATTTTATAAT  
TCCCTTTAGGAGGATCACCTAAGTGAAGACTATTTTACCTAAGAAATGT  
TAAATGTAAAGACATGGTTGTAATCTGGGGATTCTGTAAATGGCTA  
GCAGACAGAAGTCAGACGACAGGCTAGAAATGTGTGAAGAGTGGTGCCT  
TTGAAAGGCGGAGTTGGTAATGATTTTCTTCCATTTTCCATGCTTTCCA  
ATCTCTACAAAGGCCTTAATATTACTTCGATAACCAGGACCTCTGATAA  
CCTGCCCCCAGGAGTAAAGACTTAGCTGGGAAAGTCAGCTTCATGTGAG  
GTAAAAGGAACCAAGTAATACACAATCCCACTGCCAAGTGTGGGTGTG  
CAGGCCTGAGCTTCTGCTGTGGGAGGAAAGAGAAAGAGAGAGAACT  
CCAAGATCCAAGAGATCCAGCAAGAAGGCTGGAGTCTGAGGACGCAGAAA  
GCTGAATGGCACAGTTACCACTATTGTGCTGAGGTCTGTGGCCTCTGGG  
TCTCTTGACAACTGGGCAAAGACCCACAGAAAACTATCTCTAGACCTAC

FIG. 4 (21 of 61)

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CTGTGGGAGGGGAAAGTCTTCAGATCACTACAGGACAGCCACCTGGAA  
CTCAAATGGCTTACAGTTCCTTCATCCAGAGGGTCTTCATCTAGTACATA  
CCAGGTGCTAAGCCTGGGTGCTGGAGACATGACGGGGAACCCATTTACCA  
TGGCTTTGTACTGTGACATTACATCTAGGGAAAGCCAGCAAAGGGGAG  
GGATCGAGGAGAGCTTGTAGGCAGAGAAAATACCCAAGGGCAAGGGAGA  
AGCCAGCCTGTTCTGAGCACACACAGTGGTTCATCTAACTGGGCCTCAG  
TGCCAGGTGGACTGGAGATGGGGCTGAGGAGCTGTACAGAGCATTCTG  
GACACAGATGTCACATAGTCCCCTTGAGGTTAGGGTCTTAGGCATGGCAG  
CATTTGCTTTGAGTTTTTCTTTTGTAAATGTTGCCATTATGACAATGTGG  
AAGATGGGTCTTGCAGAGAAGGGCAGGGCTGTGAGACCAGTTAGGAGAC  
TAAGATGTGAGCCAAGGAAAATGAGGAACACCTGAACACTGGGGCAGGTG  
CAGGGCCCAGAGAGAAGCAGATGGCTTCCTGAGGTTTTAAGTAGGTAGAA  
TCAAGGCAGCTGGTAAAGATCTTTTATTACATATAAACTGGAATAAGCCA  
TCTGCTCCAAGACAAAAGAGTAGGCGGAAAACAATACAAGACAGAAATGG  
AATTAGAACAAACCTGGGAGGAATGTGGAATTAGAGTAGAGAGTCCAACA  
CTGGCTGCAATCATAAAAATGTAAAAACAAACAAAATTTGCTAGGTGTGC  
TTACTTAGAAATAATTAGCTGTCTATTAAGTTCACTTGTGTTATGGCTT  
AAATGTGTCCCCAAAATGTGATGTGTTGGAACTTGATCCCCAATGCAA  
CAGAGTTGAGAGATGGGACCTTTAAAAGGTGATTAGGTCTAAGGGTTCT  
GCCCTCATAAATGAATTAATACTGTTATCATGAGAGTAGATTCCCTGATAA  
AAGGATGATCTCTGCCCTCCTCCCCACAGCCCTCTTGTGCATGCTTTCTG  
CCTTTCCACCTTCTGCTATGGGATGACACAGCAAGAAGGCCCTCACCAGA  
TGCAGCTCCTTGATCTTGGACTTTCCAGCCTCCAGAAGTGAAGCCAAAC  
AAATTTCTGTTTATTATAAAATTACCCAGTCTCAGGTATTCTGTTCTAGAA  
GCACAAAATGGACTAAGATCATTAGATTATCATTTTTTATCAGACTGTTG  
AAGTGAAAAATAAAAATCAAAATAAGAAATTAAGAGAGCTGCATGCAGCA  
GCTCATGCCTATAATCCCAGCACTTTGGGAGGCCAAGGCAGGTGGATTGC  
CTGAGCTCAGGAGTTTCAGACCAGCCTGGGCAACACGGTGAAACCCCTGTT  
TCTACTAAAAATACAAAAAACTAGGCCGGGCGCGGTGGCTCACGTCTGTAA  
TCCCAGCACTTTGGGAGGCCGAGGCGGGTGGATCATGAGGTGAGGAGATC  
GAGACCATCTGGCTAACAAAGGTGAAACCCCGTCTCTACTAAAAATACAA  
AAAAAATTAGCCGGGCGCGGTGGCGGGCGCCTGTAGTCCCAGCTACTCGG  
GAGGCTGAGGCAGGAGAAATGGCGTGAAACCCGGGAAGCGGAGCTTGCACT  
GAGCCGAGATTGCGCCACTGCAGTCCGCAGTCCCGCCTGGGGCAGCAGGC  
GAGACTCCGTCTCAAAAAAATAAAAAAACTAGCCAGGCATGGTGGTGT  
GTGCCTATAGTCCCAGCTACTTGGGAGGCTGAGGCAGGAGAAATTGCTTGA  
ACCCAGGAGGTGGAGGTTGCAGTGAGCTGAGATCATACCACTGCACTCCA  
ATCCAGCCTGGGTGACAAAGCAAGACTACATTTCAAAAAAAGAAAG  
AAAAAGAAAAAAGAAAAAGAAATTAAGAGAAGGGCAGGTATTAA  
CCCCAAATATCCACCATAGGGACACATTAAAGTTTGTCTGGCCACTCCC  
CTAGCATATATATGGAATGTCTTCAAGGACCCTCTGTTGTAATAACAAG  
GCCCTGCTGGACTTAATACAACCTGCAGGCTTTGAGATCCCTACTCTGTT  
GCCATCTCTCATAGGATTTGCAGACCAATCCAAATACTTAAATAGCAA  
CACTCACAAACATGCAATCAGAGCAGAAAAGAACTTCTAAAAGGCCCT  
GAAACTACACTTTATGAGAGAAGACATAGGGACCTGAGGGTGGTAGAAT  
TTTCTCTCTATGCATCTATGTTTCCAGGGCTCACTTTCTCAATAAACTCT  
TAAATTGCTTTTAAAGTAAGGGAACAAGCAACATTACATTTAAGAGAAA  
TCAATTTTCAAAAGAAAGGGGGATGTCCAGGGTACTTTGCTTCCATGTTT  
TGCTTCCATGAATTTGTGTTTAAACAGAAGATGCAGAAAAACACAAATTA  
TTGCAAAATCAAGGAAATCCACTCTAAACATCCCTTGGTTTCCCAGGCCA  
GTGTCACAACTGAAAAACATATTGTGGCTAATTATGTGTCACAAATTAG  
AATGACAAGGCAAGAAAAAATACTCTCTGATTAACTAATAGCAGCCAA  
CACAGACAGCCTGTGTAGCTCGACTCTGCTGGTTTATAAAGGCAGAGA  
AGCAAAACGGCTTCTGTGACCGCAACAGGAAGGGCCTCTGCTCTTAATAAA  
TAAATAACATTTAAATTATTCTCCCCCATTTGCAAGCATTTTCCAACCTC  
ATTATCTCATCTGACCAGGTATTATTGTATCTGACCAAGAACTTGTATAC  
NAAATAAAGAATAAAAAATAAATATGGGCCANGCACAGTGGCTCATGCTT  
GTAATCCCANCACTTTGGGAGGCCAGGCGGGTGGATCACTTGAGGTCAG  
TAGTTTGAGACCAGTCTGGCCGACATGGCGAAACCCCGTCTCTACTAAAA  
ATACAAAAATTAGCCCCGCATGGTGGCAGATGCCTGTAATCCCAACTACT

FIG. 4 (22 of 61)

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TGGGAGGCTGAGGCACGAGAAATTGCTTGAAGCTCGAGAGGCGGAGGTTGCA  
GTGAGCCGAGACTGCGGCCATTGCCCTCCAGCCTGGGCGATGAGAGCGAA  
ACTTCATCGAAAAACAAAAACAAAAACAAAAACACCTTAGAAGA  
AGCGTTCTCTCTTGTCTTCTGAAGACACTCTACGCTGAAACAGTAACT  
TTCAATAAACCATCTCTTCTCACCACACTCTGCGACTTGCCCTGAATTC  
TTTGTGTGCAAGATCCAATAAGCCTCTCTTGGCGGTCTGGATGAGAACCT  
TTTGTGGAATACTCTGACACAACAAATTGCAGAAAGAAAGTCTCACATG  
TATAAAATAAGCAAAAAGATTCTCTGGCATCTGAAGAAACAAATTCCTTG  
TCAATATTAGTATCACTATAAGTGTAGAACAACCTGTTGTATGATGCTAC  
ATAAAGTATATGAATCTGAATACTGTTGGATACAAAGGGAGACTATNNAA  
TGTAATACGTCGCCCCGAAATGACTACACTGTTGGTGATCTTTCTTTCAAG  
AAGCANAATATTGCCTCNAACATCCTGTACATGGTATAAAATTTTA  
>Cont1g44  
CCCAGCAAGAACACCAATACAACGGGGGGGGCGTTCTTTGTGAGGGGTGG  
GGAGGTCAATTTTTTGGAACTGCAGCAGGTAACACACAAAACTTCCACA  
GCTGCTACCAGCTTTCCAGGAGAGCCTGTGTACCTGGAGAGGGAAGGCA  
AGTGCTTCCGAACCTTGACTTGATGTCTTAGATTCTGCAATGCGTAGTCTG  
TAGGGACAGGCTGTAGCTTATCCTATAGGCTTGGGCTGGAGTCAGCAAGC  
ATCTGGGCTGGCAGAAGATAAAAGATGCAAAGGTGGAGGAAAGCATACGT  
GGTCTGGAAGACAGACTTGGTGGGTGGGTGGCTGCTACAACACCCTAGTT  
AGAGGTAGAGGGGTAAAGTCAGTGTGTCTTCTGCACAGGCCTCTTCCCCAC  
CTCATTCTTCATTTCCCATACAGCCTTGCTGAGTTATTACAAACATCTG  
ATTCAACTGGAAGCTGGGTTGAGGATGACCTAAAGGACTAGTGTGATGCC  
TGCCCAGGGGTGTGGGCCCATAGTCAGAGTCCAGAGCCTCCTCTCAGCTT  
TTAGCACATCTCACCACATCCTGGGTCTTAATTAGCAATATGAAAGCA  
AGCCAAGTGACAAGATTTTGTCCCTGGGAAGTCCAGAAGCACTCCTTTTC  
TCATTTGTATAAGCATAATGATTTGCTTACATAAAATAATCATGAAAATTC  
AAATCCCTCTCAGAAATCAGGTCAATAAACCATGAAATGCAGCATGTGGG  
CAAGAATCACAGGGAAGGTAGGTCTTGGAAGAAAGAAAGGATGGCAGGGAG  
GAAGAAAGCAGGGGTGCCAGGGGCCCTGGGCTGCTGTCCAAGTCAGGTGGC  
TCACCGTCTCTGAGAACATTTCACTTTCTGGTAAATGGGGCAGTTGGAGA  
TAGAAGGGTTGGGTGAATGCCAAGAGTGAGCACAGCTGAGGTCAGTGCTG  
TGCCTGCAGTCCAGGCGGGAGTAGAAATCCTGGGCCCATCTTACCTCCGA  
CCTCATTCTCTCTCTGTAATAATGTGGGGGTGGGGGAAAGTTCTGGTCA  
TCAGCCCTAGCATTCCATGGTTCAATTCCTCATCAGTGATGGAAAATCAC  
CAAGCAAGAGAACAGGATGGAGAATAACCGATGGGTGCAATCGGAGGTG  
CTATTTCAAGGTGAGGTGGCCAGGGAAGGCCCTCTGAAAGGGTGGCTTGAG  
CAGGTGGCTGAATGTACAGAAGCTGCCAATCATGAAAGATCTGGGGTACA  
GCATGCCAAGCAGAGGAAATGCGAGTGCAAAGGCCCGAGATTGGATGTG  
GGCTTAGCACAAATGTGGCATGGCAAGAAGGCCAGTGTGGCTGAAGCAGC  
ATGAACAATGGGTGGAGGGGCTGAGAGGACAGAGGAGCAGGAAAGAGCCA  
GGCTTGGGTAGGAGAGGTGTCAACTTGATATATGATGCAAAGCCCTTGA  
GGTTCCCAACACAAAAGCAATGATCTAATATATGGTTTTAAAAATGCCA  
CTCTTGGCCCGGGCGCGGTGGCTCACGCCTGTAATCCAGCACTTTGGGAG  
GCCGAGGCGGGTGGATCATGAGGTGAGGAGATCGAGACCATCCTGGCTAA  
CAAGGTGAAACCCCGTCTCTACTAAAAATACAAAAATTAGCCGGGCGCG  
GTGGCGGGCGCCTGTAGTCCCAGCTACTCGGGAGGCTGAGGCAGGAGAAT  
GGCGTGAACCCGGGAGGCGGAGCTTGCAAGTGAGCCGAGATTGCGCCACTG  
CAGTCCGCAGTCCGGCCTGGGCGACAGAGCGAGACTCCGTCTCAAAAAAA  
AAAAAAAATAAATGCCACTCTTGCTGTGAAAAATTGACCTGGGGGA  
AGGAGGAGTAGAAATGTCAAAGTGGAAGCAGACCACTCAGGAGGTGAGG  
GCAATGGACTGTGCAGGAGAGACTGACATCTTAGACTCGGGCAATAGGAG  
AGAAGGTGGTGAGGATTATATTCTGGGCATAAAGGCAACAGAACTAGCTG  
ATGGCGTCAACGTAGGAGATGAGGGAAAGAAAGAAATCAAAGGGCATTCA  
TAGGTTTGAGGGTTGAGTAACTGGGGATATTTAACAGAAATGGAGAAGTC  
TGGGGAAGGGGCAAGTATTGTGGGGCAGGGGTCAAAGTCTGTATTTT  
GGCCAAGTTAATAATTTGAGATACCTCTTAGGTGTCCAAGTGAAGAT  
GTCAAACAGTCAATTGAATACAAAATCTGAATCTTAGCCCAGGATGGTCT  
CACACCTGTAATCCAGCACTTTGGGAGGCTGAGGTGAGAGGATCACTTG  
AGGCCAGGAGTTTGTGATCAGCCTGGGCAATAGAGCAAGACCCTGTCTCC

FIG. 4 (23 of 61)

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ACACACACACACACACA. AAAAAGTCATCCAGGCATGGTGGCACATGC...  
GTAGTCCCAGCTACTCAGGAAGCTGAGGCAGGAGGATCACTTGAGCCCAT  
GGTTCAAGGCTGCAGTGAGCTATAATCACATCACTCAATACTACACTCCA  
GCCTGGATGACAGAGAGAGACCTCATTATTAAATAAAATTTAAAAAAA  
TTAATTAAAAATAAATCCAAATCTTCTGAGATTCAATTTCAGGAGTAA  
CTGTCACTGTAGAAGGCATATAATGCCATGGGTACATGATACCATCTAAT  
GAATGCCACTGGAAAAGAGAGAATAGCTAAAAACTGAGCACTGGGCACAC  
CAGCACAGTGAGGTTTGAAGGAAGAAATGGAGCTAACAAAGGAGACAAAA  
GAGGAGTAGCCAGTGAGAAGAGAGAAACATCTGGAGAGAAGAGAGAGCAG  
CAAAAGGTGGGTGAAGGAGAATGTGGTCCACCAGGCCCAACAATGCTGAG  
CAGTTGAGTAAGTGAGGACCTGGCCACTGAATTTGGCAAGAAAGAGGATG  
TCAGCGGCCCTAGAACCAAAAGTGAAGAAGAGCTTGAGGACGGAAGCCTGA  
CAGGAGTGAACCTGAGGAGAGAATGAAAGGTGGAGACATGGAGCCAAGGAG  
CACTGAGACTCCCTTGAGTAGTTTTGCTGTAAAAATAAAAGTGAGTGCGA  
GACGGGGCAGGGGGACAGAGAAATGCAGGGGTAGCTGGAGGGAGCCACAG  
AATCAAAAGAGGGTTTTTGTGTTTAAAGATGGTAGTTGTACATAGCACAT  
TAGTAAGTTCATGTGAATCACAACGTAGGTGAGACAGATCACTAATGCAG  
GAGTCAAATCCTTGACAGAGCCCCCAGAGGAGGTGATGAAGGGAAGTGATG  
GACATCATTGAGTGAAGTAGGTTAGCAATTCCTGGGTACAAATAGGA  
GGTGACTCCTTCTGATTGCTCCTGTTTTCTGAATGAGATAGCACATAAA  
GTCCACTCAGCCATGTTAGCTGTTGAAGTCCTTGTGGCTGTCATGCCTGT  
ACAGACTGGGCTCTCCTCTCCAGCATTCTCTCAGACTAAGCTGAGCTG  
CACTAGCCGCTGCCACATCCTCTTGGGGCCATCCTCTGCCACACTCCACA  
TATTGCTGTGGTTTGTCTTGAACCCCTGGAAGGTCTACTGGCTGCTCCT  
AGAAGAGTCTGGGCGGCATCTCTCCCTTACTCGTTATCACATGGTGCTGT  
AAGCAGTGGCCACACACTTTAGCTGGTGGGATGGGCCATCACAGGCAGTA  
AATGCCGAAAGACTGCTCAGATTTTAAAGCACCATGAATCAGTAGAATGA  
GTTTAGAATTGTAGTCATCAACACACATTAAAAAAGGATTTAACTACAAC  
CCAGATAGGAGGTGCAAAATTGTCCTTACATAAATCAGATGGAAAAAGTT  
GAAAGCAGATAAGATAAAATAGGTAAGCATGACATTTAAAGGTATTTCAT  
GGGACGTGGTTACAAAACCAACTCAAACTAAAAAGTCTTAGGACCTCTC  
GCTGACTTAGGAGCCTGATCCCACTTTGAGAATGACTCAGTGTTTACC  
CTGTGGCTAGTGTAGACCAATGATCCTGTCTCAGAGTCACTAGCCAACAG  
CCCATATCAAGTAATTGAACTTTGACTCAGAAACCTCAGTGTGAGAACC  
TTTGACTTAGGAACCACCTGTAGTGGTTAACTGCAATTTGCACCCCTTAG  
TTCAGGGCTTTACAACACCGGGGGGGGGGAGGGGGAAGGCATAGAGCTGA  
TGACCTAAAGGAAACCCATTGCAGCAACGCTTTTGTGTTAAGTTTACAAA  
TAAGTGTGTTTGTAGAACTCTCCAGGTAATGCCTTTGTTATTTAATGTGT  
CTGAGACAATTCTGCACATTAAAGAATATAAAATATTACCTTGTAATTCC  
AATTTGAAATGTGTAATTGACATTAGACTTCTATTTTAAATTTGAAATGTC  
TAAACAATGTGGTTAAGTTTGTAAAAGGTGTGTGAATTTTGAGTCTGAT  
TTACTACATTTTTTTTTTAATTTCTTTTTTTTGGAGTTTATAGGGATTGC  
TTAGATGGCTAGAAAGATCGCTAGGCACATGTCC

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GATGTGTGACGTGTGTGCAAAATACCGTGCCTTTTTGTTTTCTTTTGT  
GAAACAGAGTCTCACTCTGTGCGCCAGGCTAGAATGTAGTGGCGTGATGT  
CAGCTCACTGCAACCTCCGCCTCCAGGTTCCAGTGATTCTCCCGCCTCA  
GCCTCCCAAGTAACTGGGATTACAGGCGCCACCAACAGCCCGCTAAT  
TTTTGTATTTTAGTAGAGACGGGGTTTCACCATGTTGGCCAGGCTGGTC  
TCTAACTCCTGACCTCGAGATCCACCCACCTCGACCTCCCAAAGTGCTGG  
GATTACAGGCATGAGCCACCATGCCTGGCCAATACTGTGCCATTTTATTA  
TCAGGGAATTGAGCATCCATGGATTTTGGCATCCATAGGGGTCTGTAAAC  
CAATACTGCACAAATACCAAGGGACAACCTGTATTCTAAAAAGACCAAAAA  
TTAATAAGCAGGACGCTGAAGGTAATTGCCCAATAAAGTCATGATCCCT  
TGCCCAAGTGTCTGAACCTCAGCCAGTTTTCATACTCAGGACCTATTGGCT  
GCAGAGGTGGTAGGAACCATATGAGAATCTGCAATATCATGGCAAGTAT  
GCACTTTAATGATATCTGCAGTCTTCCCCAAAGGACCTTACATTTACC  
ATACTGCTATGTCCTGCGTGAGAGGGTAATACTCAGATTTTTTTTTTTTT  
TTTTTTTACACAACGCTCTTACTGTGTGGCCCACTGGAGTGCATGGCT

FIG. 4 (24 of 61)

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CGATCTTAGCTCACTGC .CTTCTGTTT .TGGGCTCAAGTGATTCTC:  
GCCTCAGTTTCCTGAGTAGCTGGGATTACAGGCGCCCGCCACCATGCCTG  
GCTAATTTTTGTATTTTTAGTAGAGACGGAGTTTTGCCATGTTGGCCAGG  
CTGGTCTTGAACCTCTGACCTCATGTGATCCGCTGGCCTCCCAAAGTGCT  
GAGATCCAGCGTCCGCGGCCATACCGGCGGGAATTCTTTATATATTC  
TGAAAACTAATCCTTTGTGAGACATAAGTGTTGTAAATATTGTATCCAG  
TTTGTGGCATGTATTTTTAATTTTTAATGGTGTCTCTCAATGAAAAAAGC  
TTAACACTTAAATGAGGTCAAATTGATCACCTTTTTATTTATGGTTGATT  
CCTTTGGTGTGATGTGTAAGGAATGTTGTTCTTCTGTCCCAAAGTTGC  
AAAGATTTCTTGTGTATTTTGTCTAAAAGTTTTAAAGTTTTGCTTTTCC  
CATCTGTGCACATTTACATTTGCTACATCTCACTGACTGCTTCCTCTGC  
TGCAGAGCAAGCTCCATGAGAGCAGGAGGCATGGGTCTGCTTCTTGTG  
GTCCCCAGAGCCCTATGTCATGACTAGGACCTGGCAGGGGACTAGTGAGT  
AGCTCCTGACTAACTGACTCAATGAATGAATGATTGGATGATTGAACAAA  
GTGGTATGGGAGTTCACAGCGAGTAAGAGATGCCTTAGAAGAGATGAAGA  
AGGAGATGGTATAGGGTAGTGGTTCTCAATCTGGGTCCATGTTGGACTC  
ACCTGGGGACCCTTAAAATGTACCGTGGAGGATCCAGCCCCAAGAGATTC  
TGTATGACTGGTCTAAGATGTGGTCTGGGCACCAGGTGATCCCAGTGTGC  
AGCCAGGCCTGAGGCCACTGGATTGTTGGTGAATGAGGTAACTATCAAG  
GGTACAGACGTTGGTTGCCAACAGGCTTGGGCTTGAATTTAAGCTTTGTC  
ACTGACTTGTGTGCTCCTGCACTCGTTGAGCCTGTTTTCTCAGCTGA  
GAGATGGGTGTGATAACACCTACCTGCTGTAGTTGTTGTGAGAGTTAGAG  
GAGATAAGCATGTTCTTGAATGAAGTGTGTTCTTAATCCATCATAGGTT  
TTTTGCTTGTGTTGTTGTTGTTGTTGTTGTTTTCTTTTCAAGAATGA  
GGTTGAGCCAGACTTTGACAGCTGGGTGGGAAGTGAACATGTGGTGATTG  
GGAGAGAAGGGCAGTTTATGTGAAGGAATGTAATAATTAGAGAGTGGGC  
GTGGGAAGACATGCTGGGGAGAGTGAGCAGGCCGGTTAGCCCTGGTAGAG  
GGTGCAAGAGAGCAGTGCGGAATCTGCCAGGGAGACAGGTGGGTGACCAG  
GGTGCCAAGGGTGTGGCTTTTCCCAGGTTCCCATGGACACAGCCATCCTC  
CCAGATGCCCAGCCTAGCTGTGAGTGAGCAAGAGTTCTGGATTGTCTCTC  
TCACTCTGTCTTTTTCTCTCATTCCAGAAACAAAGCAGTGACTGGTACTT  
AGGAGGAGAATCAGGTCAAGTTGGGAGAACTTGCTTCTGCTCAGGGGAG  
CAGAAGCAAGAATGGAGGCCACCCATGCTGGAAGATGATGAGGGTTTT  
GGTTACGGGAGGAGGAATATTGGGGATCTAAAGGGGCCTGGGAGTGGGGC  
AGGACCCCTGCCTTAGGACAGGTAGAAACATTTCTATAAAAAATGGGGTG  
GAGGTTGATGGTAGGACCAGGCATCTTTAGTTGGCTCCCTGGAGTGTCAA  
GCCCTTGAGATGGTCTTTAAAGCCATGCAGTGGGGTTTGAATCTGGTGT  
TCAAGCTCATAGGTTATTAACATAATGACACTTGGAACTATTTGGGAGA  
GCTCAAGTGAGTGGCCTGGAAGTTCTGTGTTGGTGCAGGAGGTGACTTAG  
GATGTGCTGCTCAGACTCATATCTTTGACTGCACACCTGATGCTTCATC  
TGGCTATCCTGTAAGCACCTTCAACTTAACATGTCTACACAGAACTCTT  
GATATTCCTGTTCTCCCCAGTTCCTCAGTTCCTTACCAAATGTTCTTCC  
AGTTACCCAATTGCTCAAGTAAAAAATCTAAGTCCTTCTCTTGGATTTCT  
GCCTGTTCCCTCAACATCCCACCTATCCATGAGTGTTCTGTGGGCCCTGC  
CTCTGAAATAAATCCTGCCTTTGTCTCCAGTTCCTCCAGCCACCCATC  
CTGGGGCTGCACCCTCCTCCTTCCAAGCCCTCTCCCTTTCTTCTGTTG  
CTGCCCTGTGATGTCAGCATATGCATCAGTGCGACCAGGACATTTGAAAT  
GCAACCAGTACAATTGGGCGCGGTTATGCCTACCAGTTTTTCTTCTTAA  
ACATTTTATATTTATGTTTGAAGCATGCCACCTTTCTTCACTTGCCAAC  
TTGACAGATTTATTAGTTGACAACATCCGCTGATAGCATCAGTAATAAGT  
TAATTGTTTTTGCACATGTAGCTTTAATTATTTCTCATTATCATTTATAGG  
AGTTATTCTTTGTAAAGGGTAACTGAGTTTTCCAAAACAAACAGAAATTT  
GGGGTGGGCCCCAGTGGAGCGTGACTCATGAAATCAGATTCTTAGAAGGACC  
TCGGCAAGTCTCTGGGTGCTGTTAATGAGCCTGGCTGGCTGCCAGGGGT  
GTGTCTGCCCTTTATGAGGCCACCACTGTTCAAATGCTTGCCTGCAGCAT  
TACTTGCTAGGTAGTGCTTGTCTTACTGAACTGTGAGGGATCCAATTC  
TTTGTGGTCTAAGTAACAATACTCAGATTCACAAGGAATTGATTAATAAG  
CCAGAATGCCAATGTATTACATTTTTGATGAAGACCATATTTACAGTGAT  
TGTATCTGCTCAAGCTCAAATTAGGATTAGAGTTCTGACAAATACATATG  
TGAGAAGTATGAGGTTAAATACTTGAAATTTGGACTTTTCTAGAAAATCT

FIG. 4 (25 of 61)

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GAATGTGATTGCCATTACATACCTTTCTGGGGATGATGATTCTTGTACT  
TTTATTTTAAAGACATAGAAAATAAAGTAAAGATCAGATTGCTTGGCT  
GGGCACAGTGGCTCATGCCTGTAATGCCAGCACTTTGGGAGGCCAAGGTG  
AGTGGATTGCTTGAGCTCAGGAGTTTGAGATCAGCCTGGGCAACATGGTG  
AAATCCCATCTCTACCAAAAAATACAAAAAACAACCAAAA  
AGAATAAATTAGCTAGGTGTGATGGTGCCTGCTTGTAGTTCCAGCTACTT  
GGGAGGATGAGGTGGAAGAATTGCTTGAGCCAGGAGGTGGAGGTTTCAG  
TGAGCTGGGGTTGCAACAGTGTACTCCAGCCTGGGCGATAGAGTGAGACT  
CCGTCTCAAAAAAATAATCAGATTGCTTTATTGCTGGTTTTCTTTCT  
AAAACAGATTGGGTCCCATCATCCCCTGGCCCCCATTTGGTTAATGGTT  
CCTCCTTTTGTCTATTGAATAAAAAATACAGATGTCTGCTTTTGGCAACATGG  
TTGAATGTAGACACTGCAGGGTCTTCTGACTCAAAATGATTTAGGCTTA  
GATAAAACACATTTGGAAATGCATTTCTGGATTAAACCAAGGAAAGGAG  
ATCTCTTTAAATCCCTTTCTGTTCCCCCTCCCTACCCCTCCAATTGG  
GCTTAAGTAAGAGGGTGGTTACCCGCTAGTAAACCCCTTCGAAGGGGG  
TCTTCTCTCTAAGGGAAAACCCTTGTTTTGACATTTGCTTCAATGGGCC  
CTTGATTTTGTTCCTTGCTAAACGGGTGCTAAACCAGGGGCTCCTCTT

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AAGGCTTTTAGAATATTTGCACACTTTAGAAATGGAAATGTTTTTGGGGG  
GCGAGTTGTCTTAATATTTTCTAGCTTGTGTGACATCCTTTTGA  
AAGCAGCAATTTCTGGCCTTTGTGAGAGATGGTGAATGCCTGCAGGTGTGT  
GGACCAGTGCCTCCCTTCTTCTACATGCACGGCCCCCAGCTGGGCCCCA  
GCAGAGTGTCTGTACAGAATAATTTCCAAGGGCTGTGTCTTAACCTTTG  
GTCTTGTCCCCCATTTGCTGTAGATTTGGCCAATTGACTTCATAAGTGCCCT  
CTTATGAACATAGATGTTGGCAATGGAAGTTGAGGACCAGTCAGTGTTG  
TTTTATTGAACACACAGCGTAAATCCCAACACAATGCTGACCTAAGAGAA  
TTCCAGCCACTCTGATTCTCAGTCTCTTTATATCTGAAAGGGTTCTGTTT  
CACTTTTCCCAGATCAAAATGTCCCTGCAGCTACTCAGCAGAGCTGTCTG  
CAACTTATACGTAGAAGAGGTAACAGTCCACAAACAGAAAGGCACAGGAC  
GAGAGTGGTCTGGGTGATGCTTCTGTGGGGGAAAAGGTGATGAGGGTGC  
ATCTGCACACCTATGTTTCATAGGTAAGTCTGGGAGGAGGTGACCTCCCT  
TTGGTTGAGGTGCTGAGGCGTCTTGTTAGAATGGCACTATTCCATTATC  
TGATGCAGTCTGTGGGAATTTTGTGGTATGGCCACCACAGGTACCATGCT  
GGGAACCAATGCCAGATACTGCCTGCTAAGCCACAGCATGAGTCACATGAG  
CATTTGTGGGCTTTGGGAACTAAAGTTATTGAACGATAGTTATCTGAAAA  
GGAATTTAGGGAAAGGGGACTTTAGTCCAGCGAACAGTTTGCAAAACCAGG  
GGGAAGGCAGCCTTCAGCGTAAATGAAGACGTGTGTGCCCAATAACA  
AAGGGAGAGTTTGTCTTTTAGAGAGTAAATGTCCACGCAAGGTTCCACTT  
AGGCAATGAAAGATGCAAACTTGCTTAGTTCTGATTTGTTTACATTTGC  
TGAATTCGGATTGGTCCGTGCAGGCTTTTCTGGGAACTCCAAATACATGT  
ATGACCTCTAGTCATACATGGCAAATGGCCGCTTGGCTCTAATTTGAATT  
TAGGCCCAGTTAGTCACTCAGGATTAACCTTTTTCAGGGTTCACAGCTCT  
GAACAATGGACTTAGACCTGCAGGACATAATCTGTTCTTAACCTCTGGGAC  
TACCTGTGCCTTTTGACTGTGCCCAGTGAGCAGCTGTGGCTCTGGGCCCA  
GACCCACAGGGCGATAAGGCCACAGAGGTACGATGGAGCAGGCTGTCCCT  
GCTGAGTGATCATGAAGATACACTTACATAGAGCAGCACTTTTCTTCCA  
GTCTTTGTGATTTAACTCATTAGATCCTTATAACAAGAGTCAGTCCTCTA  
TTTAACCCATGAAGCACAGGTGGAGTCCAAGCTTAGTTTGTGAAGGATGA  
GCCAAAAGGATTCTTCTCTGTAGACCTCAAGCTCAGCTCTCTCCATGGG  
CCCTGGAGTAGGTGAGAAGGCCTCTGTCTTCCAGAGCCCACTGCCAATCA  
TCTACATTTTCTGTTAGCCCAATTCTAGGACATTGCTTTACCACTGAAG  
GGTGAGAATATCATAAGTTATAAAATCAATTGAAAAACAAGGTAC  
AGAACAGAAAAATAAAGATGAGAATCTATTAAACATAGTGATGTTACTGG  
AAAAGGGGGTCTCAAACCAGACCCCAAGAGAGAGTCCTTGGATTTACAC  
AGGAAAGAACTCAAGGTGAGTTGCAGGGTGGGTGAATTGAGAGAGTTTA  
TTGAAAGCTATTCCATTACAAAGTAGAGCATCTCAGACAGCAAGTGAG  
GAACATGCCATCATTAAATTTTCTTATATAGGAATCTTGTCTATATAAA  
GACTAAACTAAGCTGTGGCTATGTGTGGGTGGGCCGACAGCATGAAAACA  
TTTATTCTCCTATTGATTTAAAGAGAACTATCCTTGACATTTTAGTGTGT

FIG. 4 (26 of 61)

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TTAAGTACATCAAAGCA1AACTATAATTA2CTTGAAAGCATATATTTTAA  
TAGGGATTGGGACATCTGGGCTTCTGTTGTTGTAGAAGTTTGTCTTGC  
AGGGATTACCAAGCCACTTCTTAGCTGTAAACATCTTAGGGCCATGGGT  
CCTGACTGGCAAGGAATGTGTCTTGCTAGTTTTTAAGATGGGCTTGATTG  
AAAATGGTGTCCATCTGGCTCTCCTAGGCTCCTGCTTCTAACAGTAAG  
GGTAAATGCTATGTTATGAAATGTCAATTTCTGCCTTTAGCTTGCAAACCTC  
TTGATGGTGAAATTTCTCCTGTCCGTTTTTCAGTGGGGTATTTATTCTGCAT  
CCACGTCTTCAACAAGGAGCTGAAAACAAATTGGATGGAAGCAACTGGGT  
TTATGGGACACGTTAATGTTTTAATGTCAATTTGGTGTGGAATTCAGATGT  
CCAAGCAACATTTTACACTACAAATCTGCAACTTTAATAATCACTCAAAG  
TACCTGAACCTCAATGCTTTTACAGACAGACTTGGTATAAAGCCACCACCTC  
TTTCTATTATGGCAGCCCTATCCTGAGGACACAAATTTCTGCAGGGCTTC  
TGGCATATCTCTGATTAAACAAATGTCAACAAGGTTAAACAAATGTCAT  
CTCTGATTTGTTTGTGTTTTAAAGCCTGGATTTACTCATTTGAATATTTCACT  
CCTACTAGCATGTCTTGTTAGTAGTTTTCTTCAGGGACCCTAATTATTGCT  
ATTAAAAATATGTGTGCAGCTACATGTTTTTTTTTTTATCAATTTGCAATG  
AAAACCTTTAATTTGAATAATCTATTAGTGTATTATTTGAAAGTGAAATCT  
TTTCCTTTTGTCTTTCTTGTCTCACACATAGTGCAGACAGTTTCCACAG  
GGCTCATAAAAGGAATGATTCTGCCTTGTGTGAACTTTTTGCCTTTATTG  
TTAATTGCACCATTTTGTGACTGGCTCTTGACCCTGTTGTAACCAAGCT  
CATAATGTACATTATTTCTATTTTGCAAGTTGTAGACACTTGAGGAAGTT  
CCCATTCTTTGTTTCTTCTTGTCTTTGTTCCCTGTGATAACTTTTTCATG  
CAGACATTTTTTTTTTTTTTTTTTTTGGAGACCGAGTCTTGCTCTGTCTATC  
CAGGCTGGAGTGCAGTGGCATGATCTTGGCTCACTGCAACCTCTGCCTCC  
CAGGTTCAAGAGATTCTCCTGCTTCAGCCTTTCTAGTAGCTAGGATTGCA  
GGCGTGCACCTACCACACCCAGCTAAATTTTTCAAATTAGCCACCCACCT  
GGCTAATTTTTGTATTTTTTAGTAGAGACAGGGTTTCAACCATGTTGGCCA  
GGCTGGTCTCGACCAGGTGATCCACCCGCTTAGCCTCGCATAGTTGCAG  
GTGCTATTCTGAGCTCAGGGCTCTGGCAGCTACAAGCCCAAGATGCGGTC  
TCCAACATGTGGCCATTCAATGTCTAGGCGCCCTCTACTGGTCTTGGGAA  
GCGCAGCTCTGCCAGTAGCTCCAGCAGGGCACAGCTGTTAAGTCGTGATG  
TTCTACAGGTGACCAAGGGCAATCTCTGGAATCTTAGCCGCTAGGTCC  
TCTCTGTAGCAGGACCCAGGAGAAGGCAGGGGCTGAGGATGGCTCTCTTA  
GACATTTGTGATGAACCAAACGTGTGCATTTCATGAAACTTCTGTGAGCAA  
GCAGGTGAGTAGAGTTGGGTTATAAAAAGTCTTAGGGTCTCACTACAGAG  
ATGGACTTGTGTGTAGATGGTGCAGAGCCGCTGAAGAGTTCTACTTGGG  
GTAATGGTGTGATTGGGTTTGCCTTTTAGGAAGATTCTTGGCCAGAATG  
AGGCGGGCAACCCAGAGCAGGGAGTGGCCACATGTGGGTGTGCAGTTATG  
GGCCACTAATCCAGGTGATAAATGGTGTCTCTGAACTTCAGGTGGGGGTG  
CCACATGTCTCCATCTGCTCTGTACCCTTGAGACTGGCCTTATGGGCTGC  
CTTAGTGGTCTGTTGTCTCTATCTCCTGGTTGGGCTCAGGCAATGGGAG  
ATCAGAGGGAGGAAAGAGAGCTTGGTTAGAGTGCACCCGCGCCCTTTCAG  
GTTGGCAGTGGCCACATTCCCCTATACAGAAGGCCACAGTTTCTGTCACT  
GGCCCTCCACAGCCCCAGCTTTCTCAGTGGGCCAGCCACCTCCCCATCC  
CTTGCTCCTCCTCCTCCAGAGAGGGTTGTGGATTTCCACTGTGAGCAGTG  
CCTGGAGCTCCACCATCTCCTGCTGCTTCTCTGGACCTGCCTGCAGTTT  
TATAAATAACCTTTCTTACATTACCTCTAGCATGCACCTTTTGTGTGTA  
TACTCTGCCCCCTGTGAGCATGACTCATGCCAAAGAGTTTGAATTTTT  
TTCTCCAGGCAACGGGAGGTCAATTGGAGGATTTTAGACATTGAGAACAGA  
TGTGTATTGTGGAATATCTGTCTGACTGAAGTGACCAGGATGGTCCAAA  
AGAGCGAGAATTTGAGGCAAGCAAACCATCAGCAGGCCAGCAGCAAAAT  
CCAGGTCAATAACAGGGAAGCTGAGGCTCACAGGGTTGGATCAGGGAATG  
GGAGAGGGAAGCCAAACAATTCCATGAGCATGTGAGTTGCACATATGACT  
TGGTAATATTTTTATTTTTATTTTTATGTTTGGAGACAGAGTCTCGCTC  
TGTACACAGGCCAGAGTGTAGTGGCATGATCACAGCTCTCTGCAACCTC  
TGCCTCCTAGGTTCAAACAATTCTCCTGCCTCAACCTTCCAGGTAGCTGG  
GACTACAGGTGCGCACCCTACACCCAACTAAGTTGTGTATTTTAGTAG  
AGATGAGCATTACGCTGTTGCCTTAGACACGG

&gt;Cont1g47

AATATTGATTATTTGACCAGAAATTCATGCAGCTAACCGTGACCCCTGGC

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AAAATAAAATAGTGTAT...GTACGTGCAATATACATGCAAAGAAATGAG...  
GAAACTAGAAGGATGTCAATCAAATGATAACATGGTCATCTTGGGGTCGG  
AGTACATTTGGGGATGAGGGAGCTGTAAAAGCAGACTTGGACCTTTTCT  
TCTACCAGTACCGTGTCAATTTGAATTTTGGAAAGAAAAAAAAAACTCAG  
AAGGAGGAGAAGGAGCAGGAGGAGAAGAAGATGGATCTTAAGTGATTTGC  
CCGGGAGCACCTTGAGAAGGTGAGATTCAAGTCTAGGTCTAAGCTTTCTA  
ATCCATGAGTGGGAGTGACCCACGTCCAAGAGGAAGCTCAAAAGGAAGA  
TGTTCTCCATCATCTCTTGCTCATCCTAACAGCATGCAAACCACATCCA  
ATGCAGCTCAGAAAACCTCCCAAATTGCCAAATTTTCATTGGAAACACTTAA  
TGCTGTGGTTTCCAAATTTCAACTGTAAAGTAGGTATGTATGCCATTGTTA  
CCATTAACTTCTCAGAAATGGAGAGAGCTCTCTTCCGCCTCCTCCCCCT  
CTGCTGTGGCTTTGGTGAGACGTGCACTCAGGCTCACCTGTCTCCATGAT  
CTCCAGTAAGTACACATGAGCAGAGAGGCCTCAGCTCAGCTCTTCTGGT  
CCCACCAGGGTTGATTCTTTGAGAAATCTAGAATGCCACATCCTAGGCCC  
CCCAAAGAAATCCTGCATCTTACCCCCAGAAATATGAATCATAGCAAAT  
TCAAATCAACCATCGTTTAATACTCACAGACTGGGCACATCCAAAAACAT  
ATTTTCAGTTTTTACAAACAGTGCCTGGTGCATATCGGCACTATTTGTGGAA  
GCAATAAATCGACACGGAGCTGAAACACAAACAAATGCCAAATGTTTTT  
ATAACACCTGATTTTCTTTCTGTTTCTTTATGCAGTTTAGTTTTGTTTTG  
CTTAACCTCTACCTCAGACCATAGTCTGGTAAACTCACCACCCAGAAGCTC  
CCTTGAAATGTGGGTATGCAGCCACTAGGTGGCAGGAGAGAGTTTTCTGC  
CTGGAGGGAGGACAGCCACTCTGTCCCCGGGTGAGGCCAGGGCCACCCTG  
CTACCTGCAAAATTAAGCATGGGGCTTTATGAACACAGCTTCCTAATAAA  
CACAGGATCTGTTTGATAGAGACTCCAAAACACGCCTACCTAGTGATGAA  
AGACTCAACTTCAGAAGAAAACCTTCATGGCAAACATCTTCAGAGATGTT  
TCCAACCTTAAGGTTCTGAACACAGACGCTTCCCCAGAAAGCCATTGTTTC  
TCAGCACCTGGGAGCCTTGCTTTGCTTTGCTTACAGACTCGCTGTTCTTA  
AATCACTGCCAAGATAACATCTGTCTCTTCTCTTACCCTCTATTTTCGATA  
TAAGGACTCCTCACTCTTGTTGCTTCTATTGGCTACCTCTCCACAGGGA  
GAAATCGCTGATTTAACAGCAGTCAATATCCCAAATCTGGAACAGGGAAC  
AGGGAAGCATTTAAAAATTGGAGAATTTAGGCCGGGCAAGTGGCTCATG  
CCTGTAATCTCAGCACTTTGGGAGGTGACGTGGATGGATCACTTAGGAG  
TTCGAGACCAAGCCTGGGCAACATGGCGAAACCTCATCTCTACAAAAAAA  
AAAAAAAAAAAAAAAAAAAAAAAAAACCCAAATTAGCCGGGCATGGTA  
GTGCACACCTGTGAGCCCCAGCTACTCAGGAGGCTGAGGTGGCAAGACTG  
CTTGAGCCCTGAGGTGAGGCTGCAGTGAGCCGAGATCACACCACTGCAC  
TTCAGCCTGGGCAACAGAGTGAGACCTTGTCAGATAAAATAAATTAAT  
TAATTTAATTAGAGGATTTAAGGATTTTCCCTACAGACACCTCCTTATTT  
TCTCTGGCCTTTTCTGACTACTCTCCCTAACTCCCTGCTCCTCTGGTCTC  
CCAAAACCTACTCCAGAAAAAAAAGGGGGGAGGGACTAAAGGAAAGCC  
AGGTGACAGTGCCAGTGTGACAGATGACAAAGCATCTGCCCGAACAAACC  
GTAGGTCCCTGAACTTTCTCCAAGACCTGTCTGTGGACTTACCTATGAAA  
ACCACTTTTAGCAAAAACCTCCTAAGCCAGTTTATCAAGATCCCCTTAT  
CCTCAATATCCATCTGATTGGATTCTTCATCCCCCACCATTCCCCAGTGA  
TGTCACCAGGCCTTTCTTCAGCAACAGTAGTTAGTGGGTGTAGCCAGGAC  
GCCCCCTCACCCCTGATATGCCCTTTTAGTAATTCTTCATCCACAGGTTT  
CCACCCTGCTCCTAGGCTATACATTCCCATTTGCCCATGCTGCATTCCGA  
ATTGAGCCCAGTTCTATACTGAGGTCTTACTTCACCTCTCGCCATAGTCC  
TGAATAAAATTGGTTTTTACATTTAAAAACTGTCCAGCTCTGGTTGTTCC  
TTGACACAGGGTAATTTTATTCCATGTGATAGTTTGCCTTACCTCAGCC  
TACCCCCCTCAAACCTGCAACTCTATATTCAAGAACCAGACAGCCCTTTC  
CAACAGATAGGAAGAGGCTGCCCTGGTGCAAAGGAAGAGGCTCTGGGAGG  
AAGGAGAGAACCCGAAGGCTGCCCCCTCCTCTAGACTGAGCTCTGGGATG  
GGTGGACGATAAAACCCAGATACGTTTAGACATCTGAGCGTGGAGAGGAC  
TTTGCTTTGCTTCCACAGGGACCCCAAGGAACTGCAAGCCCTCCAGAGA  
CTAAAAACAGCAGAACAGCAAGAAATGGCAGCAAAGGTCTGGGCAGAATC  
ATCCTATGTGGGCACAGACACAAACAGAGTCCCCTGTGGCCCCAGGAGAG  
TTTAAAGAAGATCCAGAGGCTGTCTTATTCCATATCTCAGCAGAGACAGG  
CCCCTGAGCCTAAAAGCTGATCATTAGGACAAGAAGGACACGAACTGTCC  
TGCAGCGTGAACCGCTGGAACAAGCCAATCACCAGACACCAGACCAGC

FIG. 4 (28 of 61)

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CAGACACAGCCCCGAG1:SCCCCAAGACCACCACGGACCCATCGCCCCCTC  
ACCAATAGCTCCAGGCTACATAGACCCCCCTCCACTTCATGGATGTCCTCA  
GAGCAGAAAGGGGAGGCAGGAGTGGAAACCTGACTTGGTTCAGTTGAAAC  
ATAAAATGACTGTACTATTATTGAATTGCTGAAGTTTACGTGAAAGAAAT  
GAGATTTAGTTTTTGGCCACAGTGCAAAATAAGAAACGAGGCTTCAACTG  
AGATTAAGGTGAGTTATAGGAAAATGTACTCCCTTGAAGGACCTGTGAAG  
TGTTTTCGCTATGAGAAAATGACCAGAAATCCACGTTCTTAGCTGCGGGAC  
TCAGGCTGACTCCTGTTTCTGGAGCTTGCAAAAGGGCAGGGAAATCCCT  
GTTTCAGGCACAGTGATTTCAATGTTTAAAAGAAAACAGGTGGGCCCTGG  
CAATCATGATAACATGTCATAAGTTTACATCTCTGTGAGGCAGGTAGTGT  
AATCCCCATTTTGCAAAGGAGGAAACCGAGGCTGAAAGCAGCTACATGGT  
CTCTTCAATGTGGCCCAAATGTTGGAGAACAGAGCTTAACTGAATCAGCA  
ATTCTATACTTAGAACTGACTCTCTCTTTATTATATCTCACTACTACCTT  
GATATTTGAAATATTCAACTTTTTTCAATCAAAAAATAACAATAATTTAG  
GCATAATGACTACTATGTCATTTAATTTCTTGCTGATATTTCAATATCCC  
ATGCCAGGAATATTGAAAGCTCAGCTCCTTAAGAGCTGACTATGGCATCA  
ACTCCCAACAACCATCCTTCCAGAAATATTTTCCCCCTTCTTTTGTATA  
GAGTGGCACTGCCCTATATGGTGACCACTTGCCACATGTGGCTGTTGAAC  
ACTTGAAATTGGCTTGTGAGAATTGCAGTGTAAGTGTAAAACACATACC  
AAATTTCAAAGACATGGCACATAATAAAAAATGTAAAATATCTCATTAA  
AATTTTTATATTGACTGTGTAAGTAACATTTTGAATATATTGGATTAAAT  
ACATGGATGATGCCCCAACACCCACAGTCCCTTATCAAGTCTCTACTTCA  
CATTTTTGTACTTCTGACTTAGAAATAGCACTGGCGTCTAAGAGCCTATT  
AATGTCGTCAATAGGTTCTTGGGAACCACAATTTTAAACAAAATGACATA  
TAAGAAAACGAATAACATTGAACAAAATGACATTATTCGAGGACCTGCTG  
CATGTTGTTTCACTTAAAGTCAGTGTCCAAGAACCTATCAGTGACATTTA  
GTGAGGACTTGCTGTCTTCTGTTTACAGGAACCTGGGCAAGTTACTTA  
ATTCCTCTAAGCCTGGTTTATATCCCTGCAAAGAGAGAAGGATAATAATC  
ACCACTACTTAGTGATGTCGTAAGGAGAAAATAAAATAATAAATATGAAA  
TGGCTGACAGTGTCTTGTGTCACACAGAAGATGTGTGATCCACAGTAGCTG  
CTATTGTCTGCCTCACTTCACTAGTAATGGTCCAGGGAGGCCTTTAATGT  
GCATGGTGCAGTACATTACATGTTGGACATGGGTGAAGGGAAAGACCAG  
GCTCATCTAAACACAATAGGATGCTTGTGGTGTTTTGAGGAGGAATCAAG  
GACTAGTTATCCACAGCTGTAACATGCATGGATCAAAAGAGATAAGGCAC  
ACAAAAGACTTTGTGAGTAGCAAAGCATTACAAAATGCAGAGACCAGCTG  
TGGGTGGTGGTGAGTCAAGCCAGCTTCCCTCTGTGCCTGGCTGAGTGGT  
TCTGGGCAAGTCACGCCATCTGTCTTGATGCCCTTCCCCATCTATAGAGA  
GGGAGCAACTGAGGCCCTTCCAATACTGAAGTCCTTTATTTCTGCTACT  
TTAGAAATATCCACATTTTGGTAAATTCAAATGATCCAATGATTCCATT  
TCCTAATGTTCAAACCTAGCCCCAGAAACATCTAAATGAATCAAACAAAT  
AAAATATTTATTGTGTATGTTTTGATTGCTGAAACTTCTATTTTAGCAAC  
ACACACACACACACAGAACCCATAAGCCTTCATCTTTCCTTGGATAAA  
CGAGCCTTCTGTCTGGCCATTTAAGTCACGATTAAGTAAATGATTCCA  
ACTCGCCTTTTGACAGCAGTTCAGATGGGTCTTCTGCGTGGCAGTGGCC  
CTCCTGACTTATGATTTCTGTGTGTGCGCCTGTTACCACTGCAGCTTAA  
CTGAGGAAACAAGAACAACACAGCTTCTGACCCCAAGAGACTGTTGGAGG  
CAAAGGCTTCAGTCCCAAGAACCTCACACGTGGGGAGCCCGAGAGCCAG  
CCCTGACCTTTTCTCCAGTAATAACATAAGAAACAACAGGCCTTGGCCTT  
ATTTTGGATACAAAGAGTGGTGCTTTTCTTAAATCTTCTTTAGTCAGG  
GCTACCCCTTCATGGACGCCCAACATCCATGGTTCCTGCTTGAGTCCCT  
GCTTCCATATCTGCACTTCTCACTTGAAATATCCCTGGAGTACGTTAA  
GCAGCCAGGTTTGAAGTTCCTGTGTGACAGGCGGTGTGTGCATGTCTT  
CTCTCTCAACAGGACACAAGCTCCCCAAATCAGACGGTATGCCTCCACGC  
CCCTTCCCAAGCCTCCCCAGCAGCACCGAGCATGTGAGGGGAGCTGGGGC  
CCAGGCCATGATGGGAAGCACTCTCTGCCTAAAGACTAGGGTGTGCGCC  
CTCAACTGTGGGAATGAGCCCCAGCTCTGGTGTCTGCCTCGGTTTTCTT  
CCTGGACAATCAACATGAACCTCTCACCCTCTTATCCACTTTGCATAAA  
CTGAAAATAACAAACCCAGGGCTCTTTCTGTACAGGAAAGGGTTTTTTT  
TTATAAAATTAACAGAGATGATTCAACACACCCAGGATATAACACATGG  
GCCATGAATCAAGGGCAGCATTGCTCTGGTCAGCCTGTTGTTTGGGCCCC

FIG. 4 (29 of 61)

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CTTGGCAGGGCTCTCCCCA GAATCTTCCCCTCTTGACTCCCATCANACA  
GCACTCCANCTTTGTGTTACAGGCGATAAATGGGAAAGGGTAAAT  
>Contig48  
CATTCTTAATTAGAGAAACGCTCATTAACTAGACACCCAAATTCTCTGG  
GGGGGATCATTCTTACAAGCATGCCCTTCTCTCTTAAAGAGAGAGCACT  
TTTTTCGCAAATAATGCTGCCATGAACATACGGGGTGCATGTATCTTCGT  
AATAGAATGATTTCTATTTTGGGGGGTATGTACCCAGCAATAGGATTGCT  
GGGTCAAATGGTATTTCTGGTTCTAGATCTTCGAGATCTTCCACACCGTC  
TTCCACAATGGTTGAACCTAATTCACATTCTTACCAACAGTGTGAAAGCAT  
TCCTATTTCTCTGCAACCTCGCCAGCACCTGTTATTTCTTGACTTTTTTAA  
TAATCGTCATTCTGACTAGCATGAGAGACAGTATCTCGTTGAGGATTTGA  
TGTGCATTTTGCTAATGATCAGTGATGTTGAGCTTTTTTTCATATGTTTT  
TTGGCTGCAAGAATGCTCTTTTGGAGAAGTGTCTGTTGATGTCCTTTGC  
CCACTTTTTAATGGGGGTTGTTTTTCTTGTAATTTGTTTAAGCTCCT  
TATAGACTCACAATAACAAAGACATGGGATCAACCTAAATGTCCATCAAT  
GATATAACGGATAAAGAAATGTGGTACATATATACCATGGAATAGTATG  
CAGCCATAAAAAAGAATGGGATCATATCCTTTGAAAGGACATGGATGAGC  
TGGAACCATGATCCTCAGCAAACTATGCAAGAACAGAAAAACAATTGTTG  
CATGCTCTCACTTATAAGTGGGAGCTGAACACTGAGAACAACAGGGACACA  
GAGAGGGGAACAACACACATTTGGGGCCTGTCAGGGGTGAGGTGGGGGAG  
GGAGAGCATTAGGAAAAATAGCTAATGCATGCTGGGCTTAATACCTAGGT  
GATGGGTTGACAGGTGCAGCAAACTCACTGTGGCACAATTTACCTATGTA  
ACAAACCTGCACATCTGCACACGTACCCAGGACTTCAAAATAAAGAGA  
GACAATACTTCTCCCTTAAGTGTCTACTGTTGCTTTGCAATAAAAACTTC  
CTGCCCTTCACTTCACTCTGACTTGTCCCTGAATTCTTCTCGTGATGGT  
GTCAAGAACGTGGACACTGGCTGGGGCTGGAGACTCACCAGCATCCGGAG  
ACCCTCCTGAGCCCTCCAGCAATACAACCTTTGACACAACTATGAAATCA  
CAGATCCAAGAAGCTCAAAGAACCCAGCACAGGAAACATGATGAAACTA  
CATGAAGGAACATCAGAAATTGAATTGTTCAAAATCAGTGATAAAGAGTAA  
ATCTTAAAGCAACCAAGCAAAATATCCATCATATACGCAGAAATAAAG  
ATAAGTATGACAGCAGATTTACAAATAGAAAAAAAACAAGTGCAGCAAC  
AGAAACAACTATCAATCCATAATTCTATACCTAGTGAAAATTTCTTTCA  
AAACAAAGGTGAAATAAAAAAATTATTTTCAGGAATACAAAAGCGAAAAA  
ATTAATCACTAGCATTCACTGCAAGAAATGTTAAAGGAAGTCCTTTA  
GGCAGAAAGAAAAATGATACAAGGTGAATATTTGGATCCCTGCAAGGAACT  
AAAAAGATCCAGAACTGATAACTTAATGGGTAAACATGTAATTTTCATCA  
ACAAGTGAATGAATAAACAATCATGATATATCCATATGATAGACTACTA  
CTTAGAATACAAAAAGAAGAACTACTTATGCATGTGATAACATGAATGATA  
TTCAAAATTATTATTGAGTGAAAGACACCAGATCAAAACAAAGTACATAC  
TGTATGATTCTGTTTATATAAACTCTATAAATTGCATGCTCTTCTATAG  
TGACAGAAAGAAGATCAGTGGCTGCCTGCAGACAGGAAGAGATTACAAAC  
GGAAATGAGAATTCCTTAAGAGATGATGGACATGCTCATTACCCATCATA  
TGTATACAGCCATAATGGTTTTACAGATACATATATGTACAGCCCAAC  
ATAAATATAAGTTATCAAATTACAGTAAGTTCTGACTTAATGTCACTAGG  
TTCCTGGAACTTTGACTTTAAGCAAAATGATGTACAGTGAAACCAATTT  
TACCATAGGCTAATTGATATAAAGATGAGTTAGGTTTTTGGTTTTTTTTT  
TTTTTGACATGAAGTCTCGCTCTATCGCCAGGCAGGAGAAGAAGAGTTAG  
GTTTTACAGCATGTTTCTGGTCACAAGAACATCATCAAACCTTGTAATAA  
AGGCACAAAACACTTCTAATATTAAATATCAAAATAAATATGAGTTATAC  
AGAATTTAAGAAAGATTAATAAAAAACAAGTAAATCATTATTTATGGGAT  
TTTTGGTAATCAGTGAGTTATGTGGTCATAGTGGAAGTGGGTTAAGTCAA  
GAAATAAATGTTTGCAAAACAAAAATTTTAAAGATCCTCTCCTACCACCA  
CACAAAAACAAGAAAACACGGTGGGCTCGCTAAGCACTTTTGTACCACT  
CGTATCTTATGCGTTTGTATGATTATTGTAATGCTTTATGATAATTTTT  
AGAGACAGGGTCTCACTCTGTGTCTCAGGCTGGAGTGAAGTGGTGCAATC  
ATAGCTCACTGCAGTCTCAACCTCCCGGATTCAAGAGATCCTCCACCTC  
AGCCTCCAGTGTAGTACAGTTGTGTGCCACCATGCCCATCTAT  
CTTCTTTTTTATTTTTTGTAGAGACAGGGGTTGTGCTTTGTTGCCAGGC  
TAGTCTTCAACTCCTGGGCTCAAGCAATCCTCCTGCCTCAGCCTCCCAA  
ATGCTGGGATTTCCGACATGAGCCAGCAGCACCTTGCCAGCATTTTATT

FIG. 4 (30 of 61)

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TCATAATAATTATAAGTCATTCCTTCATTTCATCTTACAACCCACTTGTTTC  
CAGTTTCAGGATCTCGGGTGACCAGAACCTATTAACGTTTCACGCACAAGTC  
AGAAACCAGCCCTGGACAGGACACCATCTTACCGCAGGGAGAACTTACAC  
ACCCACACTCACTCAGACTGGGACCATGCAAAGAACCTAACGTGCACTTT  
GGAATGTGTGTTCCATACCCACTAGAACAGCTAAAATTTAAAAGACTGAC  
CATACTTGAGTGTGTAACAGGATGTGACACAACCTAAATCTTTTAAGCGCT  
TCGCGCTAAATGGCACAGCCGCTTTGGAAAACAGTTGGCAGTTTTTCAAG  
TTAAATATACCCAACTCTATGATCCACTTCTCAACAATCAAACAAGAGA  
AATAAAAGCAATGTCTACACAAAGATGTATACACAAATGTTTCATTGCAGC  
CTTAATTATACTAGCCCCAAGTTGAAACAAGCCAAATGTCCATTACCAGA  
TGACTGGAACATACAAATTGTGGTATATTGATACAATGAAATACTACTTA  
GTAATAAAAAAGAAAGAGCTATTAACATAAGCAACAACATGGATGAATCT  
GAAAACAATTATGTAAGTGAACAAGCCACACAAAAGTTACATACTGTA  
TGATCACATCTACATAAAATTACAGAAAAGGCCAACTAATCTATAGACAG  
AAAAGCAGATGAGTGGTTACCTAGGGATGGGGCAGAAGGGACGAAAGGAT  
GGATTGCAAAATAGCACAAAAATATTGGAGGGATGACAAATATATTTCATT  
ATCTTGATTGTGGGGATAGTTTAAATGGGTATATATAGAGATCAAAGCTCA  
TCTAATTATACACTTTAAATATATGTATTTTCATTGTGCATCAGTTATTCA  
TCAACAAGACTATAAAATAATATATGCCTACATACATTTTAAATATTCA  
AAATCTCAGCTTATATACATAAAATGCAACTGAATATGTATTTCAGATGTT  
TTAACAAGCAGAAAGGACTGATTAAGTCTATGACAGCGGCTGTTTCTGGG  
AAGGGTGTAGGAGACAAGAGATGGAAAAGAGGATGAGAGCCAGAAGAGAC  
CCTTGTAATGTTTTCTTTCTTTAGTAAAAATATATTGACAGTTAAAGCT  
GAGAGGTGAGAATAATAGTCTCATGGCTTTTGTGTCTTAAATTTTACA  
AACTAAGTGAATGGGAGAAAGCAAAAAATAAACTTAAATAAATGTTAT  
ATTGCCCAAAAAGAGATTTAAATGGAGGTTAGACACATGAGACTTACGT  
TCTCAAAAAGTAGAATCTGCAGGGAAGTTTAACTATAAAGAATTAA  
AATCTAGCTTCTACCAGCCCAAAGCCTAAATGTTCTGCTTTATTCTTCC  
TTATTATAATTATAGGTAATATATTTTATGTTTGCAAATGAATGCAGTG  
ATATTAGATCTCTAAGAGGTGCTAAAAATGAAAAGTACATATTCCAATTT  
TTCCCAATTTTCTTCTCTTCCATGAATGAAAAATATACATATTTGATG  
ATTTCCAAGTTTATACAACCGATCTTCTCTTAGTTTTCTCTTACCAAAT  
TCCCTCCCTCACTCAGCCAGCCAGTCCAACTGTGCTACCTGCACAGC  
AGCCCTCATACCATCCACACTCTCATCAGGATCCTGCCTGACCTGCGAGG  
AGCAGCAGCAAGAAGGAGACAGAACCTCCACGCTGAGCATCTCAGGGCTT  
TCTCAGAGACTCCAGAGGACCCTGATAGGGACAGAGCCTGGCCAGCAATC  
CATGCTGCCAGCTGTATGATTGTGGGCATGTAAATCTCAACTGAAAATG  
GGTGTATAATAACATGTTCTTCCAGAATGAGCTTTATGAAGATCATAT  
AGCTGTTTGAACTCAGACAAGCACTGGTAGGAATACAAACAGGGGAGCC  
AACAGCCTATAAATAACTTTAAGAAAGGGCATGAATGTAATTACTTAG  
GAACAAAAGGCCAAAGTGGAGAGATGCCTAGGACTGAGCTGGACAAGCTGC  
ACCCTTTAGTGGCTCAGCCCATGGGCTGACAAGGAAAATGGAGGAGCTAC  
CAAAGAAGGTGGAAGGATTCTGGGAGAGTGGCCCTCACCTGCCCAGGGC  
AGGGCTCAGTGGGAGAGAGGGAGATCTGTTATAAATGCTGCCAGGAGGTC  
GAGTCATGTGAGAATGTCCATGTGAAAACATCCACTGTGTGTATCTAAAG  
AGAGTGGCTGTAAACAGGTGAGGTCAAAGGTCTTATTGTCTCAGATGT  
TATCTGCATGCATTGTCTCAGACCAAGAAAATAAGGAGCATGGACACA  
AAGGGTTAGGTTGAAGCAAAAATTTAATAAGTGAAGAAGAAGGCTCTCT  
GCAGTGGAGAGGGGAGTCTGAGTGGGTTGCCACTTTGACAGCTGAATCCA  
AAAGCTTTTATAAGAACTCTTCTCATATCTGCAGCTGTTTGAGTAACTT  
CTCTTACCTATAAACTGTCTGTATAACTCTCCCTTATCTATGCAGCTGT  
GGGATGTCTCCAGGTAAAGCATAAAGTGTAGCTTCTCTGTTTGTATAACT  
GTGGGTTTGTGTTTAGGCAAGCCCCCATCCCCCTCCCTGTGTAAGCTCCCAT  
GGAGCCACCATGTGCATATCTGAGAAGTGGAGGAAGCTTTCTCTGGGAG  
CTCACTGATCGTACAAAGAACAAGAGGCTTCTGTGCCGCTTATCTATTCA  
GGTGCAGCCTGAGTTTTTCCCAGGCTGCTCTATTTTGCCTGTAGCTATG  
ATTTTTTCAGGCAGGCTGCTTCTCTGAAGACTAGCCTTAACTGTCTACCTA  
TCAGATTTTCTTTTCTTCTCTCCCTCAGCTGGTTCCCTCACCAGGCTG  
AGCAAGTGAAGAAGGAGGGCACAGGGCAGGCCAGTAGTGAGCAGCAACAAG  
GAACTAAGACAGCAGAAACCACTTTTACACCTGGGTTGAAGGGGTGGG

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GAGCCAGGACTACAGCTCAGGTAAGAACATAGGTAAAGAGATACTGTTGT  
TGTGTTGTTTTAACTATGAGAAGCATTGAGCTTTAAATTTCTACAGGAA  
GGATCCAGTTCAGACAGGAGCACCCAATATTGAGAAGAGAAGAACATGGT  
GTAAAGGTCCTGGGAAGGCTGAGAGGATTGGGACTCAGAAATCCAGAGCAG  
AAGCCGTCTGTGAACAGAAGAAGGACCTCCCCAGTGTAGCAAGAGGGAG  
GGAGGAGGGACAGATGCCAAGATGGTTCAGGAAGAAGGTTTGGTGGTAAA  
TGTGAGGCTGTGCTCACCTGCTGGCTTCAATTTTCTCTTTAAATGTCAG  
ATGGAATCATTGATGAAGGCCATGCCATGCAATGAAATGGCAGTCTGAG  
GCATGGAGCAGCTCCAGCTTAGCCCGTGTTAGGGTAATTATGGCTCCAA  
CCCAGGAGATGAATATGACTAGGGAAAGTGAAGTCCAAAAACAAATGGTC  
TCAAGTTGACTGTGAGTCTTCTGGGAGGCTGAGACGACAGGTGGGGTTGA  
CAAGGGAAGGGGAACCCACCTGCTGAAAAACATCAGGCTGTTGGCTGGGG  
GAGGGGTGAGGCCTGTGTTGTAGAGATGGATGGATGCCATAAGTTGGGTA  
AAGGTTTCACTCTACCCTCTGCTGGGTGTGGAAATAAAACAAAGACCACC  
CAAATGAGAACAAACAAAGACTATTTATCCAGAGCTTGCTCTGACAAGGG  
AGTCGGCAACCATCACTTGCTTGGCAGAGACTCAGAAGTAAGCAGGGGAG  
AAAGCCTCATAGCAGAAAGAAGGGAAGTCTTCATGTATGCCCTGAGTGGC  
AGCTGTAGATGTGGGTGAGTTGCAGGTGGCTAACTAGAAAATGGGGGACTC  
CTGTGTGATTGATTAGGAGCATGTTTGGCTTTCTCTGGTTGGTCCTACAT  
TGGAAGAGGGAACAAAAAATTTAGGGCAGTTGTGAGTTATTAATCAAGTG  
TTGGCCATTTTGTACTGACTGTTACAGGAGTGACTGGCTCCCTGGATTGT  
TTGCTAGAAATAGTGGTCTTCACTTCTGCAAGTCTGACTTTCTGGTAAT  
AGGCTTCTGGGTGGCTATTGTGGATAATAAGTGGGTTTCTGAGCTGA  
TTTCTGCAGATTGTGGATCAGAGTTATTTATATAAACAGTCTGACCATT  
TTCCACTGGCATATCCATCTTCCAAGAGCTGGCCAAGCTGCTGTCTTAT  
CTGTCTCCCCAGCCCCCTCCACTCTGGCTGTGAAAATACAAGCCACTAGG  
TGAGGAATGGGGACAATTGAAGACTGAAAGCTTTTCTTTGCTGGGTTTCGC  
AGAGCTGAGGAAAGAAATGACAACATCCAAGTGTCTGCCCTGGGCCAGTT  
TTAGGACTGTAGTGGTAATGCAAGGACTGTGTGAGTTTATATTTTCATTT  
GTCTCTCTAACTAAGGTGGAACAAAAAAGCAGAAAATGTCTGTCTGCA  
GTCTCTGCAAAAGTCTAACACTGTGCTTCCCAACATTGCAGCCATTAGCC  
ACAGGTGAGTATGAAAAGACTTTAAATGAGACTGGTCCAACTGAGATGTG  
CTCTGAGAATAAAACACACAGCAGATTTCAAAGACCTAGTACATGCCCTG  
ATTTCAAGCTATATTACAAAGCTGTGGTAATCAAAACAGTATGGCATTGG  
GAAAAAATAGACACATTGGTCAATGTGACAGAATAGAGAGCCCAGAAAT  
AAACCCGTGCATGTATAGTCAACTAATCTTTGACAAGAGTACCAAGAATA  
CACAATGGGGAAAGTCTCTTCAATAAGTGGTGTGGGAAAACTAGATATC  
CACATGCAAAAGAAAGAAATTAGACCCTTGATTACACAAAACTTAAAT  
TAATTCAAAAATAGAAAAAGACTTACATGTAAGATCTAAACCATAAACT  
CCTAGAAGAAAACATAGGGAAAGAGCTCCTTGACACTGGCATTAGCAGTA  
ATTTTTCAGATATAACATCAAAGTACAGGCAATGAAAGCAAAAAACAAGT  
GAGAGTATATCAAACATAAAAGTTTCTGCACAGCATAAAACAATCAACAGA  
GTAAGACATGACGTATGGAATGAGAGAAAATATTGACATCTGACAAAGG  
GTTAATATCCAAATATATAAGTAATTCACACAACCTCAGTAACAAAAGCC  
AAATAACCTGACTTTTTTTTAAATGGGCAAAGTACCTGAATAGGTATTC  
CTCAAAAGAAGACATACAAATGGCCAAGAGATGTATGAAAAGCTGCTTAA  
CATACTAATCATCAGAGAAATACACAAATCAAAACAAGATATCATCTCA  
CACCTGTTAGAATGGCTATTATTAATAAATGAGATAAGTGTGGCCAGGT  
GTGGAGGAAAGGAAACCCTTGATACATTATTATAGGAATGTAAATTAGTA  
CAGCCATTATGGAGAACAGTATGGAGATTCCCTAACAAAATTAATAATAG  
AATTACCATATGACCAGCAATTCCACTTCAAGGAATACATTCAAATACT  
ATCAGTATCTCAATAAGATACTTGCACTCCTATGTTCTGTCAGCGTTAT  
TCACCATAGCCAAGATACAGAAACAAGTTAAATGTCCATCAACAGATAAA  
TGGATAAAGAAAATCAGGTACATATATATATACAAATGGAATATTATTAG  
CAAAATCCTGACATCTGAGATAACCTGGATAAACCTGGAGGACATTATGC  
TAAGTAAAAATCAAAGCCTGACACAGAAAGACAAATACCACATAATCTCAC  
TTACATATGAAATATGAAATGTAAATTTTATGGAAACAGAGTAGAATGG  
TAGTTGCCAGAGCCTGAGAGTAGAGAAAATGAGATGCTTGTCAAATCAA  
TCATCACATTGAATATATATAATCTATTGTCAATTAAATATTTAAGAA  
TAAAAATACCTGGCACCAAAAAAGAATGCAAAATGTCTCAACAATGTT

ATATGTATTGCATTTTG. AGTGATAATAATTTGAATATTAGGTTAAATAA  
AATATATTTGAAAAATTAACCTTACCTATTTCTTTCCATTTTGTGTTACA  
TAGGTACAAAAAATAAATTACCTATGTGGCTCATGTAGGTGGCTC  
ACATTATACTTTGATGACACTATACAGGCTGGTGACCATATATCTCTTAG  
ACTAGTCTAAGTGATTTAACAGTGGTTCAGAAAGATCCAGGTTTAACAC  
CAATGAAAGGGCCAGCTGGCTTAGCCAGCTTGTGTGGGAAATGTTGGGG  
AGTGGTTTAAGACAGGGAAAAGCAAACTTTTGATGCTATTGACTTTTTG  
AAAAATCTTTTGTGGCTGAAAAACCAAAACATTATT

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GCTCGAGTGTGTCTCTAAAGCCTTTCCCCCATTGGCTCCACTATACGCAC  
TCTCCTGGTTTCTCCCCCTCTAGCCGCTGTCTTTGGTCTCCTTTCTGATT  
TTGCTGCGTCTCTGTCCCCCTGAATGATTGCTTCTCCACTACGGGGTGAT  
TTTGCTCCCCAGGGGACATTTGGCAATATCTGGAGAGGTCTATGGTTGTG  
TTTGAGGGTGTGCTACTGCCATCTAGTGGGGAGAGGCTAAAGATGCTGT  
TAATGCCCAGGACAGTCCCCATAACACAGAATTATTGAGCTCAAAATATC  
CATGTTGCCAAGATCAAGAAACCCTGCTCAAATATTAGCATGTGCTGAAG  
GCCCTTCTCTTTCTTTAGCAATATCTGCCTCCTTAGGGATCTTTTCTAG  
TCTCAGTGGTTTAAACATTTAAATCCCAAATTAGGCAATAAATTGGGCCC  
CAAACCTCGTTAGTATAAAATGTAGAACTGTGTTATTAGAAGGCTAATAA  
AATGACCTGGTGAGCATCTGCAGCTAGCCTCTGAGCAATTCTGGGGACCA  
CGTGCAAGATAAATCCATCTGTTCCCTCTCTGTAATGTGGCGCTACCTTG  
TGGCCGATTTTCTCGGGTTAAATATCTCTGGGGATGCAACTTGTCTGTG  
GTTAATGGCTGTGTGAGGCCAGCGCTGGTGATAAAGGAATCAATCAAGA  
CAATATTGAATTTAGAAAGGCAGATTTATTTAGAGAAAAGGAGAGATACG  
TTGCAAGGGGAGCAATGGGCAATACAGCAGAGGGAAGGCTGTCTGCAAAGA  
GGCAAGGGCTACGTATGACGTAGGGCTGCTTAGGCTGAATGCTTGACAGAC  
AAGATGCTTGCGTGACAGGTGGGCTGTGAGCTGAGTGCTTGGGTGCTAGTG  
AGCCATTGGCAGCTGACCCTATTTCTTGAACATTGCTCCCTGCAAGCA  
TTTTAATGTTAAACCGCCAGGTGAGTTGAATTTCTTTTCTTTTCTTTT  
TTTTTTTTTTTTTGCTTTTAGTAGGACCTGCCGTTGTGAGACTATCTGAGG  
TAAATTAGACACCCTCCTGGTTTAAGTCACCGCTCCAGTGACTAGGCAGG  
GAGCTCTTCTTGAAGAGGGTGTGGGCAGTGGGTACTTTGCATGTTGTCC  
ACACCAGGCGAGCTGCTGCTTACGGGCTTTCATTTGCTCTTTCTTTG  
CCCAAATGCACTTCTCTCACTGTTTACATGATTTTTCTCCCTCTTTTCC  
TTTTAGTCTTTGTCTAAATATCACCTTCTAGGGAGGCTTCCACACCAC  
CTCTTCAAGATTTGAGGGTATGCACCCCCACCCCTAGCCTTCTTATCCCT  
CTCCACTGCTTTCTTCTCAAAGCACTTGTTACGTTCAAATAAAATAGATT  
AGTTACTTTATAGTTCTAATTTTACTATTTTTTGTGTTACTTTCATCAATAC  
CCATGTAATCTCTGGAAGGAACGTTTCTTTTGTAGTGTATTTCTAGCAC  
CTAGAACAGTACTTTGGCACATGGCAGGTGTTCAAAGTATTTGTTGATTA  
TTTTCTCAAAGGGCATGGAGTCTTAGAAGTTTGAGAACACAGTTCTAAGC  
ACAGCTGTTTAGAGACTATGGATGATGCTAATGGCTGTATTTCCAGTAGG  
TGGGGCAATTTCTCAAATTGACCTGGAACTCTTGAGATCTGGGGACAGTCA  
CCAAGCACTGGGCTCTGTGGGGAGAGATGTGCTGGTTTTTAGAGAGGAGA  
ATAGCATCCTGGGGGACTTGGCCCCAGGGCTTCTCTGTCCCAATCTCTTC  
CCAAGTGAAGTCCAGAGGAGGAGGCTTGTCTGTAGCTGGTCAAGTCTCTG  
TAACTGTTTCCCTCCCATCTACACAGATGCAAAGAAGGCTGAGAAAAGCA  
AGCTGTGAGGTGAGCAGGGGCCCTGACTCCTCCCAGAAAGGCACTCAGAA  
CTTCCATAGGGCAACTGGAAGAAGGTTCTACTTCTCACGGCAGCTGT  
TGCTGGGGAAAAAACCAGCCTCAGGCCCTACCCTGTGCTGAGAACCTGAA  
TCCAGTATCAGGTTCTCCAACAACTTGGATCCAGCTGACCCTCACAAGG  
GGTCAATGCAACCTTGTAGCATATGGAAATGGCAGCAAGGTCCTTGTG  
TGGACTATGCCTAGAATCTAAATTAAGACAAGGCCTCAGAGGGGCTAAGT  
GACATCTGTCTCAAAGTTTTCACAGCTAGTGTGTGACTAAATCTTGATTC  
CACCTCTCAGGTTTTACCATATCCCAAAAAGGTTGAAACAAGAAAAG  
TTATCTTTGGGCAATTACCTCTTTCTGTTCTTTGCTTTTACCTACTAATGT  
TCTAGGCTCACCTCTGGTCTGCAATCTCACTGAACTGACAGATCCCTCA  
TGGCCTAAAGGGTTTTCACTGGGTTGACTAGGCTCTCCCATGCTGT  
CCTACTGTCTAAGGCACCTCCTGGGTAGGGTGCCAGCGTCATTCTGATG  
CTGCCTGACTTTCTTCCAGCTACTTTTGAACTTGGTATCCATGGCAGA

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GGCTTAAAGGGCATGTTCCAGTACTTTTATTTCCAAATCCCCAGTGGU  
ATCAAGGAAATCAGCATCTCTGGATAGCTCTACTAAGGCTTAGTTCTCAT  
TGTCCAATCTAGCTCCTGGGTATGGGAGGCATTACAGGAAATATTTGAGT  
GTAAGAGTGAGTTGCTTTACCTCCAGAATATCCTTCCAATGGCTCTGAAG  
CAGGCTGTGGAGTCTCTGCTGGCTGATCACAGTTCACAGGTGGCTCCCAA  
CCTGTGGTCTACATCCATCTCTTTGTGAGTGTCACTGCCATTGTCCCACAA  
ATGTCATTTGGGCTAGCCCTGGGATAGTAATCAGTCTTTACATAGATA  
TACATTGTGCTTTACATCCACAGTAATTTGAGTGGACCTTAAAAATAAT  
TCCATGTGAGGTCTCACCAGCCCATGGGTTACAGATGGGGTTACCTTTCA  
GCCTTGTAAGGTGCCCCGTCTTTGAGTGTAGACATGGACTCACAACGAG  
CCACTCCTGCTGTTTCTCTGCTCTTGCTGAGGCTTCTGCTGCTGCTGCTG  
CTGCTTTGACAGGCTGGCCAGCTGTGGTGCCTGAGGCACCTGTGTCTTC  
ACAGCACCACCTTGATGAGTGGCCACGGTGTAGTTGGAAAGGGATGCTTA  
GATGGGAGGCCAATGGGAGTCTGCTTCAGGAGCAAATCCAAGTCACAGAG  
ATCGAGTCACCGAGAGCATAGTAAACTCAAAATCCCTTCTCTGCTGTTAAT  
AACTGAGATGCTGTCACTGGGTAACTCACCAGCCCTGTTTGTGCTTC  
ACTTAGAGTGATTTCTGTCTTAGAAGGCTCCTCATATCCTTCTGGGGAAG  
GCTTCTAGTGAGTCCACAGATAGCTGGACCAGGCATGTCCAGAAATAATC  
TGATTCTCACATTTGAGTTAGCCAGCGTTCCAGCTATATCCCCATTTTG  
TGTCTATATAAGTTACCAAAGCCCAAGGATATTAGGTGGCTCCTTAGT  
TTGCTTTATGATTATGCCTTGTGTGTGTGTGTGTGTGAGTGTGTACGCCCT  
ATGAGGATTCTTCTCTCCCGTTCTTGCTATGGCTTCTCTTCCCACCTGA  
TGGGCTGTAGTTCCTGTCTTTTGACTTTGGGCTTAGTCATGTGACTTT  
TTTGCCAAGGGAATGTGGGCAGAAGTAACTGGGAGCCAGTCCCAAGCTAA  
GGCCTTTGGGAAGCATGGTGAGCCTATGCCAGCTCCCTCAGAACTCCTTCC  
CTTGGCCATGAAGAGAGATAAATCTGGATTGTACCTTCAGCCCATGTCTT  
AGAATACAAACATGGAGAATAATGAACCTGACTCAAAGGCTGAAGGGCAG  
CTGAGCCCATATGAGGTCAATTGAACTGCAGCTACCTACAGACCTGAAAG  
TGAAATAAACATGTATAAGTCTCTGACGTTTGGGGTTTGTTTACATAGCA  
TTATTGTAGCAGAAACTTAAATAATACTGGGGGCTAAATATAGTGGACCA  
GTGACAGCACAGAAATGGTAAAATGGAGTGATTGTTACTTACATCACAACC  
CTTCATCTCTGTTGATGGACACTAAATCAAAGTGGCAATTACTCAGAGT  
TGGGAGTCATTGAGTTGCATCTTGTGTTTGAAGTACCTTGACAGTTTGA  
GCTCTAAGTGATTACAGAGATGGTTTCTCAGCTACAGGTAAATAAACAA  
AGGCACAGAGAAGTAAAGTGACTTCTAGAGGGCTTCATTGATATTTAGCA  
GCAGAATCAGAGCTAAACAATGAGTCTCTCATCTCCAGCCTTTCTATTCT  
TGTTTTCTAGGTTGGGATTTTGGGAAATAGTGCAGAGAGATTAGCAGTAG  
TGACATGGAAACAATGTGAGCCTCAGCTTCCATCCCTGAGGCTGCCTTCAT  
CTGCCAGGGAATGTCTCTGTGTGAGCCTTGCCTCTGACACAGATGTG  
TATGGCCACCTGAATAAGTGTCTTTTACATAGCAGCTAATGGATTGAAATG  
SGTGCTAGAGCAGTGCTTCTAAAAACTCCATGTATTAATCATCTAGGGGT  
CTTACCAAAAACGCATGCAGATTCTGATTGAGTAGGTCTGGAGTGGGGCT  
TGACATTCTGCACTTGTAACACATGGACCACACTTTGAGTAGCAATGTAT  
TAGATCATTCCAGTGGAAACATGTATGAGTGATGGAATGAACAGATATAA  
TTAATCCAGGTCTGGTAAGTGAGGTACTGATACATATTAAGTTGAAGTGA  
ATTTACATCAAAAATAATGGTTACACAGTGACTTTACTGCCCCCAAT  
TCTTTCTTTTGAGTGGTTTCAAAGTGAAGTACAGCCAGCCAGGTTAAAGT  
CCTGGTTTGTGTGTGATTAGAAGATTGATCCAGCTTTCTCTCTCTCTCT  
AATTCTTTAAATATGCAATGGCCTTCTAGAACTTGTCTCTCAGGCTCCC  
CATGAGCCACCTGTCTTAATATCTTCCCCCAGGACATTTCTGGGTCA  
AGGAAGGAATCAGGCATAGGAAAGTAGAAAGGTTGCCTGACAGTGAGA  
AACTTTTTGCACTCCTATTGTTCAATTCTAAATGTGGGTATTGTTGGG  
GCTTCTAATTGGAATCTAACTGAAATTCAGGCATGTCTAGCTATATATG  
ACCAAGAATTAGGATGAGTTCACAGAGAAGCCTATTTTTCAGGAGAGCGGT  
AGTTAAATTGAAGTTTATGGGTTTATGGTAATGGGTTGGGGAGTTTACTT  
CATTAGCAATAGCAACGTTTTTGAATCAGAGAAGTGATTTTGAACACACT  
GTACATAGTTTTCTCACTTAGATTAATCTCTGGGTCAACCTTGTGTTGGAC  
CTATATATAGAACTATTAGTGAAGAAAGGTGGGTGTCATTAGGAAAAGA  
GCCATTTATTCAAATGTTCTGTGTTGACATTAGGGCACTGGCAAGACTACA  
GAATCAATAGATATTTAAAAACAGCCAGGTGCGGTGGCTCAGGCCTGTAA

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TCCAGCGTGATTTGGC .TTACTTTGGGAGGCTGAAGCGGGTGGATTG  
TGAGCTCAGGAATTCAAGACCAGCCTGGTCAACACGGTGAAACCCTATCT  
CTACTAAAATACAAAAAATTAGCCGGGCATGGTGGCAGGCGCCTATAATC  
CCAGCTACTTTGGGAGGCTGAGGCAGGAGAATCGCTTGAACCCAGGAGGCG  
GATGTTGTTCATGAGCTGAGATCGCGCCATTGCACTCAAGCCAGGGCAAGA  
ATAACAAGACTCTGTCTCACAACAAACAAGCGAACATACGAAACAAACGT  
AACATCCAAACTAGCAGGTACATGCCGTGCCAGTCATGACCCATGGTCAT  
AAGATGCTTACAGCTCAGGAAGCAGCTGCACAATGCCTGCATAGACAAAC  
TCTTATGAAAGCAGAATGTCTGATGTCTCCATAACACATAACAGTGTAT  
GCTTTTATTATGGTCATACTCTAGCTGTGATGTACCTACGCTCTAATATG  
CCAACGATAGTTTCTTTAAATCATCAACATAATAAATGTCTATGCTGTCA  
GTCCCCCACATGTAGACATAACTTAGCTGGTACATGGATAAGAAACCTAT  
ATTAGATAACCTTAGGCCAGGTGTGGTGGCTCATGCCTGTAATCCCAGCA  
CTTTGGGGAGGCCGAGGGTGGATCACGAGGTCAGGAGATCGAGACCA  
CCCTGGCTAACCAAGTGAACCCCGTCTCTACTAAAAATACAAAAA  
TTAACCGGGCATGGTGGCAGGCACCTGTGGTCCCAGCTACTCAGGAAGCT  
GAGGCGGGAGAATGGCGTGAACCCAGGAGGCGGAGGTTGCAGTAAGCCGA  
GATCACACCACTGCACTCCAGCCTGGGGGACAGAGCGCAAGATTTCTGTCT  
CCCAACCCAAAAANCNANNNNAAATTTGCACCCAAATCTGACTAATTCCA  
GAGCCAAATCCAATTTAGAATCGTTATATCTCCCTGGTGAAGTGAAGCTT  
TTATCTTTAAGGAGACACACTCTTTATGTCTACCAATGCTTATTGECTTA  
AAGTCCACTTTGTTCAGATACAGCTGCTTTCTTTTAAATAGTTTTTGTGTG  
GTATATCTCTTCCATCCTTTTTCTTTCAGCCTTCTCCATTCTTACATTT  
TAGATATATTTCTTTTTCTTTTTTTTTGAGAGAGAGTCTCACTCTCTC  
GCCAGGCTGGAGTAGTGCAATGGCGCGATCTTAGCTCACTGCAACCTCC  
ACCTCCTGGGTTCAAGCAATTTCTCTGCCTCAGCCTCCCAAGTAGCTGGG  
ATTACAGGAGCCACCAAGCCAGCTAATTTGTTGTATTTTTTAGAAG  
AGATGAGGTTTCGCCATGTTGGCCAGGCTGGTCTCGAACTCCTGACCTCA  
GGTCATCCACCCACCTCGGCTTTCCCAAGTGTTGGTATTACAGGCGCGA  
GCCACCATGCCAGCTGATTTTAGCTGTATCTCAAAAACAGCATGGGTTC  
TGTTTGCTTTCTTTATTCAGCTTTATAATGTAAATCATTTACATCAAACA  
TCTAATACACCATGGACTGTAAAACACAGCCATATTTTATGTATGAATTA  
AAAAAACAACCAACCAATTAGTTCCTGAGACACACACCTTAACAATAT  
CTCTGTGATGTGCATAAATCAATCACATCAGTTTCTCTGCACCTCAAAAT  
TTCTTTCTCAATTTCTCAGAGATATGGCAATTTCTCTGGTTTTACATTCC  
CAGAAGCAAGAAAAAGTACACAGCTTCTTCAAGTCATGAGTAGCTTCTT  
TTTTATAGCTCTTGGTGTGTTGCAAAAAGATTGGAATTGCTTCACTAATA  
CTAAATTTTCATTCTGCTGCTCTGTTTCTATGACAAGTCAGAGGGCATCT  
TTTTGAAGACATTCTAAACAGCAATTAACCTCAAAACATGTAATGACAAT  
GACACACAAAACCTCACTGATGACCAAATGAAGAGTTCCAGCCAAGTTGA  
CACAAGCTGGCTGACAGAGCTTGTAAATACACACAGCTTGGCATATGCCTC  
GCCATTTAGAGATGTAAAATAGGAATAAATGTTTTCCCTTAAATCAAT  
GAAATAGAGCATTGGAAGTAAAATCTACGACAGTTATAGTGTCTTCTAT  
TCATTATTCTCATTCTGTTTCTTCTCCCCCTTGCTTTCTTTAGTTTGAA  
TATTTTCTATCATTTCATTTTTCTTCTCTACTAGTTTGAAACTTATGCATT  
TATTTTCTATTTTTTAGCACTTACCTAAAATTAATCTGTAAATCCATGGAT  
CCTTAATTTATTTAAAAAATAATGTTAATGAGTAGCTTTATTTCTCTCC  
CATCTAATTTAAGGCCACAGAACACCTTCACTTACCTCAATCCTCTCTCC  
AACTTACATGCTTTTAAATGTATATATGTTAATACCGTATACCTTTTAAAA  
CTTTCTAAAATAGCATTATTTTATAGCATGAGTGTTCAATTTACATTTTTG  
CATATATTTAGAATTTTCTTTGCTCTTCGTTTCTTCTTCTATTTATGACT  
CCCCCTCTGGGATCATTTTCTTCTACTTGAAGTACATAGTTTGAAGCTGC  
ACTATTCAATACAGTAGCCACTAGCCATGTGTAGCTATTGAAGTTTAAAC  
TAAGTAAAATTGAGTAATATTAAAAACTCAGTTCTCTTCACTCTCACTAGCC  
ACATTTCAAGTGCTCAGCAGCCACATGTGACTAATGACTACTGTACAGCA  
AACATATAGAACATTTCCATCATGGCAAAGAGCTCTATTGATAGTGTTC  
TCCAGAGTTTCTGTTCCAGGACCAAACCTGAGGGTTGGGCTGCTATTTCTC  
ATGGCCCAATAACAAGATGCAGATGAGCTGGGGAGGAAGAGAGTTTTTAT  
TTCTGCAACCAGTTACAGGGAGAAGGCCTGGAAATCATCACCAGGCCAAC  
TCAAAATATGACGTTTTCCAGAGCTTATATACCTTCTAAGCTATATGTC

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TACGTGTAAGTGTGCATLACCTGAAGACGTAAGTGATTAACCTCTTTTAA  
ATCTGTAACCTAAGGTCTGAGTCCGGAAGATCTTCCCCTGGAGCCTCAGTA  
AATTTACTTAATCTAAATGGGTCCAGGTGCTGGGGTAATTACCCTTATCT  
TGTCCTCTGCTAAATCATGGAGGTTTGGGGAATTCCTTTTAGAGCACCAT  
TAACCTGTTTGTGAAGGCCTGGGAATTTCCCTCCAAACCCCCATTAAACC  
TGTTTAAATCCCAAATTGGTTCCGTTAAATAATTCCTCCTTAATTTGTCCA  
ATTTTAAAGGCCCAAAAAAGGCTGGGGCAAACCTCCTGAATGGCCTTTGTT  
ACATTTCAACCTTTGTTTAAAAACACCGGTTTTTAATATTTAACTTAACC  
ATTTAATCTCTACTGAAACACTTGTATATAAATCTGCATTAAATGAGAAC  
TGGCCTGCGCCATATCTCCTTCTCAGAAATATCTTAGGGTTGTGATCCCCT  
GTGTGAAGAGATATATCTCTGGAGATCTCAATCTCTCTACCCCAAAAAA  
AATCTCACTCGGAGAAAACCTCAGACTCTTATCTCCACAGCGCTATCTCTC  
TCCTCTCC

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GCTTGTCTAAGATGGTGCTCCTTGTGCTGTGCCTGCTTTCATCCTGGGA  
TCTCCCTTCACCATCAGGATTGCCTTCACCTCATTCCAGTCTTGGATCTT  
TCTTCTTGTCTTCTGAGTATTTTTTTTTTTTTTGTGCTGATTCCCTTCA  
GTGGCCTCTTGGGAAAAGATGTGTAGGGAGAAAAATTTCTTTAGAAACT  
TGCAATCTGACAATATATTTATCCTATCCTGACATTGGTAGATAGTTC  
AGCTGGGTACAGAATCTAATTAATTTTCTTCTGATTATAAGACATT  
GCTCCATTTTCTTCTGGCTTCCAATATTGCTGCTGAGAAGTCTGACACCA  
TTCAAATGCCTGATTTTTTCCATGTGATTGTTGTTTTCTGTCTGGAGTGT  
TGTAGGATTGCCTCTTTATCTACAGTGTCTGAAATTCATGACGTAGGT  
CTTTCTTCATTCAATTATGGTAGACACTCAGTGGGCCATTTAATCGGGAAA  
AACATGTGTTCTTCAAGTCTACAACTTTATTACTTCTCTTTTCTTGTG  
TCTTTCTCTGGTCTGTTTTAGCCCCGAGTCTCTAGATCTGTCTCTAA  
TATTCCTATTGACTTTACTTCAATTTCTAAGTCTTTATCCTTTTGCTTTA  
CTTTCCGAGAGACCTGCTTAACCTTATCTCCCAACTCTTTTATTGAATTT  
CATTTCTTTTACTATATATTTTTTACTTTGAATACACCTCTCTCTTCTC  
ACATTTTCCCCCATAGTATTTTGTCTTCAATTGACAGTCTACTATCTTA  
TTACTCTGGAGATATTAATAAGTTTTTAAATTTTATTTATTTTATT  
TTCAAAACAGTGTCTTACTCTGTCACTCAGGCTGGAGTGCAGTGGTGTGA  
TCATGGATCACTGCAGCCTTGATCTCTGAGCTCAAGCTATCCTCCTGCTT  
CAGCCTCCCAAGTAGCTGGAACCAAGGCATGTGTACCATACCCAGCTA  
ATTTTTTTGTTTTTGAGGTGGAGTCTCACTCTGTAGCCCCGGTCTGGAGTG  
CAGTGGTGCAATCTGGGCTCACAGCAACCTCTGCCTCCTGGGTCTGGTT  
CAAGCAATTCTCCTGCCTCAGCCTCCTGAGTAGCTGGGATTACAGAAACA  
CACTACCATGCCAGCTAATTTTTGTATTTTTGTAGAGACAGTTTTCAAC  
ATGTTGGGCAGCCTGGGCTGAACTCCTGACTTGTGATCTGCCCACTTGG  
GCTCCCCAAAGTGTGGGATTACAGGCGTGAGCCACTGCACCCGGCCACT  
AATTTTTAAATTGTTAATAAAGACGAGGTCTTGCTATGTTGCCAGTATG  
GTCTTGAACCTCGTGGGCTTAAGTAATCTTCTGCCTCAGCCTCCCAAAGTG  
TTGGGATTACAGGTGTGAGCCACTGAATCTGACATTTTTTAAAGTTTTTC  
TTCTCTTTACCAAGTCTTTTTTCCCCTTTCTGCTTTTTTGGGTGTTTTTA  
TTTTGATCTCTATCTTGCTAGAACTTTCTGGAGACGTTTAGTAATACTA  
GATTTTTGAGATGGGCAACTGGAAAGCTGATTGGAACTCTGAATACAT  
GGGTGAGGCTTGTGGCTGTGAGTGTCAATTGCTTGATGTCTTGGCAAGGC  
CAATGGGTTTGGGACCCCTACTATTAGTATAGGCCTGATTCCCTGGGAAA  
GGCTCTTTTGATCTCCTGCCTGGAGGATAAAGGCCTGGCTACCAGCCTTC  
TGTGTGTAATGTGAGGGAGAAGGGCTGGAGTATTCACATCATGCTGAAT  
CCTTTCAATGATCATCTTGTTTTTAGTAATCTCCTACCTTAACCTCTCTGT  
CTTCTGCTAGTATGGGAAAGATGACCTGAAATCTAACCATTTATTTTTTC  
CCCCATTAATATCATTTTATGATTATTGAGAAGTTAAATAATTGTGATGC  
TGTCCTCCAAAAAGACTGAATCAACTAGCAACAAATAAGAATTTTCTCAC  
AGCTCTGCCAGCATTTTAAAGAATAGCTTTATTGAGCCCAGGAGGTCAA  
GGCTGCAGTGAGCTGTGATTACACCACTCTACCCAGCCTGGGTGACAGA  
GCAAAACCTGTCTCAAAAAAGAAATTTAAGGAACAGCTTTATTGTTGTA  
AAATAGACATACAATAAACAGAGCACATTTTAAATTGTGCAACTTATAC  
TTTGATATAACCTGTGAAACATCACCACAATCAAGATAGTGAATATAT  
TTATCACCTCCTGATACAGTTTAGCTCTGTGTCCCCACCTAAGTCTCATG

TTGAATTGTAAATCCCAATGCTGCGGGGAGGGGCTTTGTGGGAGGTGAT1G  
AATTGTGGGGGTGCACTTCCCCCTTGCTGTTCTTGAGATAGTGAATGAGC  
TCTCATGAGCTCCCTTCACTCACTCTCTTCTCTGCTGCCATGTGAGGAT  
GTGCTTGCCCTCTTCTTTGCCCTTCTGCCATGATGTGTTTCTGAGTCCTC  
CCTAACCATGCCTCCTGTACAGCTTGCAGAACTGTGAGTCAGTAAATCT  
CTTTTCTTCAATAAATACCCAGCTCAGGTGGCTTTATAGCAGTGTGA  
AAAGGAACCTAATATACCTCCTAAGTTACCTCAAGCTTCTTCTTAATTCCT  
TCTCCTCCCTTCTTCAATTGCCAAGCAAACAACCACCTGTTTTCTGTCAC  
TATAGATTAGTTACATTTTGTGGGTTTTTTTTTTTTTTTGTAGACAAGGTC  
TCACTCTGTTGCCCAGGATGGAGTGCAGTGGTGGCATCATAGCTCATTGC  
AGCCTTGAACCTCAGTGTTCAGTGGTCCCTCCCACTTCAGCCTCCTGAGT  
ACCTGGGACTACAGGGGTACAGCCACCACAACCTGGCTTAAAAAATTTTTTA  
AATAAAAAATGGGGTCTTGTTATGTTTTCTCAGGCTGGTCTCGAACTCCCTCG  
CCTCAAGCAGCCCTCCCTCCTTGGCCTCCCAAATTGTTGGGATTACAGGC  
ATGAGTCATGACTCCTGGCCTAGTTTACATTTTCTAGAGTTTTGTATAAA  
TGGAACATACAGAATGTATTTTTTGGCGAGTGGGGGAGTGTTTCTATT  
TCTTCTTTCTTTTTTCTTTTTTTTTTTTTTTTTTTTTTGTAGACGGAGTCTCG  
CTCTGTCTGTTGCCCAGGCTGGAGTGCAGTGGTGGCATCTCGGCTCACCG  
CAAGCTCCACCTCCGGGTTCAAGCAATTCTCCTGCCACAGCTCCTGAG  
TAGCTGGGACTACAGGCGCCGCCACCACCTGGCTAATTTTTTTTTGT  
TTTTTGGTAGAGACGGGGTTTACCATTGTTAGCCAGGATGGTCTCGATCT  
CCTGACCTCGTGATCTGCCCGCTTGGCCTCCCTAAGTGTGGGATTACA  
GGCGTGAGCCACCGTGCCCGGCCCAAGTGTCTATTCTTAACCAGCTT  
TCATGCAATCTTTTTTATTTTACCATTCTCTGTGATCCCACTCCCAAAG  
TACTAGATGTGATTGGTCTTTAGGATCAGTACCATTTGCCCCAAGTGT  
TTCCAGCCTTCCAAAAATTTTTTCTTTTTTCTTAAAGATACTCCTGTG  
TGAGGCTCAGAACTCTGAATTGCTACTGCAAATATGAACTCGGTGATGT  
GAATGCCAGGGAATTGCCTGATTGATCAAAGAAATGTATCCCTTCTCCC  
TCACTCTTGCTGTCTTCTCATTTGTTTTCCCATCCTTGCGATTCTGTA  
ATTTAAATATCCCTTTAATGTTATAATATTTAATGGCGTTTGGCGAAAA  
GTACAGAATTAGGTGCAAGAGTGATAGCTGTTATTTTTTTTTTGGCCTC  
TGAGACTGTTCATATATGCAAGTATTTTAAACAGAAAGTCTGCGAGTGA  
TGAGATGTGAGGGGGTCTGATAGATACGTTTGAAGGCAGTTACTGGAA  
AAAAATAATGCCATTTCTGGTTTGTACTTCGGTAAGTTAGATGACCCAA  
TATATTGTTACATGTGGCATTAGTAAAAAAGTAGCTTCCCTCCCTTT  
CTTCTTCTTTTCTCCTTTCTGCTTCTATAAAGCATCTGCTTTGGGAAA  
CTTCTTAGGAGGAGAGCTTGCCAGCCCGTGGGTAATGGAGAGGTCTTGCA  
GAGATAAAGAGATGCTCCCACTCAATGCAGGATGGTGTGGAGGTAATG  
GGGATACGTTCTGCATCACTCAGGAATGGCCTTCTGGCAGGGAAGAGA  
AGGGAGGGGAAAGAGGAAGGGAGTCAAAGATGAATTGCTGAATACGGGA  
TTCCAGGGCCTGGAGCCAGGAAGAGAACTTTGGGAGGTGTGAACCTGGAG  
GGCATCAGCTGATGAGGAGCAGCCTGAAGTCCGGGGAGGACCTGTTTTTG  
GTGGCCAGGAAGAAAGTGCTTCCACACACAGGGAGGCCACAAGGCTGAT  
GGGCTGGGGTTGGAAGGACAGCCCTAGGACAGGCTTGGGAAGCAGGCTC  
AGGTAGGAGTCCGAGGTTCTTGTTAGTCTFTTTTCACTTCTGGTCTTAG  
AAAATAGAAATCCAAGGCTCTTGAGAGTGAAGGTTGGTTGGGAGAGG  
CAATGAGGGCTTAGGCCAGGACACCCGTAGAGCTACTGCCCAGCTGTCT  
CTCAGGGACTCTGCTGAGGTCACCTCAAGGATCATTCTTAGCCTTGCTAG  
ACAGTACTGACAGAGGGAACCGTAGTATCGCACCCACTTCTTCTCTTTC  
AATGAAAGTTTAAAGGTCACCATTTCTCTGGCAAAGGAAGTTCCACAA  
TATTCATTTCCGGTCTTAGAAACAGCAAGGTATCAAGCAATTTGCAAACT  
TCCTGTGCTGGGAATTCCAAAGGAAGTAGGGGCAGAGTTCTGGTGGAG  
CAAAGTGAATTCGAGTGATTAGTCAGTAGCAGTAGCAGTAGCAGTAGCA  
GTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGC  
AGCAGAAACAGAATTTCCCGCACGTGTCTCAGGCTCTCATTGGCCAACT  
CAGTCTCTAAGTATTTTTATTGGCAGGAAAAATAAATAGCTATGAGTGA  
AATAATTCATTAGACCTGAGCCTCCATCAATTTTGTGTTTTAAAGGCTCA  
CTCTCTTACCTTTCCCTGGGATGGAAGATGCAAAATGTTTCTGATGTCA  
TGTCAAAAAAGAAAGAACGATGGGTATATTGTATGCTTGAGTTCCAGCCA  
TTTGTGCACAAATAGATAGATGACTGCCATGTGTGTAGACTTTCTATAGA

**FIG. 4 (37 of 61)**

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CTGTGTGCTAAACCCGA<sub>1</sub>CTGCCACTTCCAAGGAGTAGATGAGGAATG<sub>1</sub>C  
CATGGTTCTGGGGAGCCCTACCCCAATTTGGGGCAGACATTCCAAAGCTC  
ATTTTCTGTGGAGGGGGTTGATGGTTAAAGGACGGCCTGGGAGTAACTCG  
TCTGTACTAGGGCCCAGGAGAGTTACATGCTGCTTCCCATGTTATTCATC  
ATTCCCCCATGTGAATAGCTATGGCGTGAGGTCCAAGGTTAGGGCCTTTC  
TACCATAAATGGGGGAATAAAATTCCCCTACCAGCCTGAGAAGTTTCTGT  
TATAAAGAGGCTTTTTTTTTTGC<sub>1</sub>GGGGGTGGGGGAGCAAGCCGACTAATGT  
GTTATTTCCATACGGTTTGT<sub>1</sub>TTTAAATGTAGATGTCATATGCAGGAGAG  
GTGGTGTAGTGAGTCACAACGGGATTAGAAGGACCAGTCCGAAAAGCAGA  
AGAGGGTCAAGTTCAGGGCACTGAGGACTACTGCATTCACTGGCGTGAAA  
GGCAGATGGCTGAACAGGAGGGGGACATTACATTGCTTGTCTCCTTGAG  
CCTCGATTTCCTCATCTAAAAAGAGGGTCATTTATTCACAGAACATTTAT  
TAAACTTGTGCCAGGCACCGTGCCAGGAGCTGGACTAAAAATTAAATCCA  
CCCCGTGAGCTGCTCTGAAGGCTAAATATGAAGTATGTAAAAGTAACC  
AAGTGTCTGACACATGCAGCTATTCAATGACTGTGTGGGCATTGCGGCAG  
ATTTTAAATTTTCTTTTATTTCTTTCTTTTAGTGAGAGGTGTTGGTTG  
TTATTATTGTCTGCTGTAAGTGTCTATTTCACTTGCTTTTGTGCTGCC  
TCCAGCCCATTCAGGGCTGTCTAAGACACTTCTTATCACCTAAATA  
ACCGGGGAGGCAAAGCGCTTCTTAAGAGATGGATCCAGAAGAACAATGC  
TGGTTTTCTGTAGAAAAAGGGGCTGTGGGAAGTAGAGATAAGAAGGGAAT  
TGGCCAAGATGAATGTACAGAGCCTTATTTTTTTTATAACACAGCAAG  
ATTAGATACAAAACAGGACAATAGCATCATCTGTTTTATAACTGGAAAG  
GACCTCACTTTACAGGTGGGAAGAATAGAGTGGAGAAGTGAAGAGAATG  
GTCACAGAGTCAATCAGCATGTCTGCGTCAAAGCTGGGATTCCCAATTCA  
GGGCTCTTACTACAGTGACGTATGGCTAATATTTTGGCATTGTTTCGGGG  
AAAAGCTGAAGCCCTGATGGTGTACGTCACTCTTGAGATAGTCTGTAGTC  
CAGCAGGGAGGAAAGCAAGGAAGGGAGGTGGAGGCAGCATTTTTGGGTGT  
AACATTTCTGTTCTTGT<sub>1</sub>TTTGTGGCCAAATCATAGTGTGATTGGGACAAGC  
CACTGCTTTCTCTGAGCCTCCACTTTCTTTTCTTCTTAAAGAGGGAGGG  
AATAGTAGAGTAAAAGTAGTCATTTTATCAAAACACCTGCTATTTTGGAGC  
CATATTGCAAGTGGGTGGGGTTGAACACTTGGCTTTATTACCCATAGG  
ATTAAATCCAACCTCGATACTGTGGCATTCCCAAACCTCAGTCTAATCTT  
CTTCTCCATCAGCCATGCCCCACGACACCCTGGTCATATCTGATGTTGCC  
CCTTGCACTTGCCCCCTCCTTATCTTTGCTTTCTGACCTACCATATGGCT  
ATTGGTTGAAATTCTCATTTTCCAGGGCCTTGCTTAAATATCATCTCATC  
CATTA<sub>1</sub>AAACTTTCTTGAACCTCCCCTTGCCCTGTTCTCCCTAATGTCTC  
AAGCCAGAATTTATTTCTTTTGTGGCCAAAGGACTGGGTTTGTGACCTC  
TCTCACGAGACTTAATATTGAGACCAAACGTCTTTAGACCTCACCAGCCA  
GAGAGATGAGCATCTATGGAATGCAGGCTTTTGCTGGACTTGCTGATGC  
AGGGCCTCTGCCTTCCCTCAGGGCCTCTCTGCTGTTTATAGGAATTTCCC  
TCATGGCACAGTCCATGAGCTCAGGGTCAAGTTCATACATGTTTTACTT  
CTTCTACTCTGCAATGGTCTTCTTGAACCTCTGAGGGTCTAAAGCTGCT  
CTGCAGTTTGTGGGGTGAGTAGAAAGGGGCTTCAAAAGTTGTGCTGTTG  
TTTCCCACCCCAATAGCATGAAACACAAAGATGCTTACAAATAGCTGCCT  
TGCTTTCTAGTCCCAACTTCTCTCTCTGAGGCTTTAA<sub>1</sub>AAACAGTCCCCT  
AGGTGAGCTGGACTGGAGTTGTATCCTATCTTCATTATCTGTCTACTCT  
CTTTCTGCTCTCTAGAGAAGATATTATATATGTGTGTATGTATGTGTA<sub>1</sub>AA  
TATATAATATCCATATATAGAACATATATTGTTATATTTACATATACATA  
CATAACATATGCATGTATTATATATACATATGTAGTATCAAAGTTGGAA  
TTAAACTGTATATTTTGAATTTGCTTTTATTTGCACTCTATCACTGTAA<sub>1</sub>A  
ATGAATATTTATCCATACCGTAAGATATTCTTCAATGTATTTT<sub>1</sub>TTTTT  
TTTGAAACAGGGTCTTGCTTTGTTGCCAGGCTGGAGTGCAATGACCCGA  
TCTTGGGTCACTGCAGCCTTGACCTCCCCGGCTCAAGTGATCTTCCACC  
TTAGCCCTCTGAGTAGCTGGGACTAAAGGTGTGTGCCCTCCACACCCAGCT  
TTTAAATTTTTTTGTATTTTTTTTAAAGACAGGGTTTTGCCACATTG  
CCCAAGCTGGTCTTGAGCTCCTGGGTCCAAGCAATCCTCCCACTTTGGCC  
TCCCAAAGTGCTAAGATTACAAGCATGAGCCACCACTGGCCTCAATG  
TAATTTTTAATGGCTGTATAGTATTCCATCATGTGGTTGTACCCAA<sub>1</sub>AAT  
ATTTAACCAGTCCCAGTTTATTTCAATTTTTTTTACTATTTTGAATA<sub>1</sub>A  
TGTTTTAGTAAATACCCACAAATATGTACAATGGCTGGGCTTAGTGGCT

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CACCCCTGTAATCCCAA...ACTTTGGGAGTCTGAGGCAGGTGGGTCACTG  
AGGTCAAGGAGTTCGAGACCATCTTGGTTAACATGGTGAAACCCCGTCTCT  
ACCAAAAATACAAAATTTAGCCGGGTGTGGTGGCACACACCTGTAATCGC  
AGCTACTTGGGAGGCTGAAGTAGGAAAATCACTTGAACCTAGGAGGCGGA  
GGTTCAGTGAGCCGAGATCACACTACTGTACTCCAGCATGGGCAACAGT  
GAGACTCCATCTCAAAAAAAAAAAAAAAAAAAAAAGTACAATTTGTTG  
TACCTCCCTGATTATTTCTTTTAAGTAGAATTTCTTATAATTTTTTTTA  
TAAGTAAAATTTTGAATCAAGGGAGAAGCACCTGGAGTCCTTCAGATACC  
TATTGCCAAACTGAACTTTTCTGTTCCAGGTTTACTACATTCAGCCTGAC  
TCAGGGTTTGGGGAGTAGAGGAGGGGGTGGAGGCAGAGGGCCTCTCCCTG  
TCCCCACAGACCTCCCTTGGTGAGGTCCAAGTCTGGACAGGTGGAGTGTG  
GCATTGCACCGTCAGGTCTGCTTCTCTGTAATTTCCCTAAATCCATCCAG  
TGGAGCCTCATTGTTCAAGTCTTTTTTTTTTTTTTTTTTTTTTAACCTCC  
CTGAAGACGGAGTCTCACTCTGTGCGCCAGGCTGGAGTGCAGTGGCACGA  
TCTTGACTCATTTC AACCTCTGCCTCCAGGTTCAAGTAATTTCTCTGCC  
TCAGCCTCCTGAGTAGCTGGCACTACAGGCGTGTACCATCACGCCCGGCT  
AATTTTTTTTTTGTATTTTAGTAGAGACGGGGTTTACCATGTTGGCCAG  
GCTGGTCTCGAACTCCTAACCTTGTGATCTACCCGCTCTGCCTCCCAA  
GTGCTGGGCTTACAGGTGTGAGCCACCAGGCTGGCCTCAAGTCTATTTT  
TTAACTCCAGGAGGCTGGTATTACAGAGGATTAGGGCTGGCAGAAGGGC  
CTCAAAGCTTTCAAGGCTGGGGAATAGGCTGCAGCCTGGTTCAGGGTAA  
CCCAAGTATTTTGGTTTCAAAGGGACAGGAAAAAAGTGATTGATATGG  
AAGTTGTCAAAGTGCAACTGTCAAGACATTAAAAATGTAACCTTTTAC  
TAATATACAGTAGACTTGTGTTAAATATTTAACTGATTGTAAGGAAAA  
AACCAGACCGAGTTTTCCCTACCATACTGTCAACAACCTCAACACTGAG  
TTCTTCTGTGACCTCTAGTCACCGAAATGCTTGGGGATTTCTCCACCAC  
TAGTCTCCAGCAGCCGACACCAGTTGGGTGTCTAATTCACCTCCAACAC  
TATCTACCTGGAGTTAGCGTTAGATCCACAGGTTGAGGGCTCAGTCTCA  
CAAGACTGCCTCCCACTTCAGGTGCCAGTTACAAGTGGTAGGTTGTCAAC  
TATGCTTCTGACTGATGGCTATAAATCTGGGTTTGTCTCCCTCGGGTTCC  
GTGAATTTGCTAGAGCAGCTCACAGAATCAGGAAAAACCTTAAGTTTAC  
CAGTTTATTCTAAAAGATATTACAAAGGATACAGATGAACACCAGATGAA  
GAGATGCGCAGAGCAAAGCATGTGAGAAGGGGTGTGGAGCTTCATGCCC  
CTCTGGGGCACCACCCTCCAGGAACCTTCATGTGTCCAGCTATCTGGGAG  
CCCTTCCAAACCTGTCTTTTTTGGGTTTTTAAGAGTGGCTTTATTACAT  
ACACATGATTGACCGAACCATTTGGCCATTGGTGACTGACACAACCTTCAG  
CCCCCTCCACTCCCTCCAGTGGTTGGGGAGTGGGGCTAACAGTCTCAAGTC  
TCCAATCCTGCCTTGGTCTTTCTGTGACAAACCCCATCATGAAGCTACT  
GCATTGGGGCTGCCAGCCAGCAGTCATCTATTAGCATGCAAAAGACACTC  
TTATTATTCAGAGATTCCAAGGGTTTTTAAAGCTGTATGTCAGGAAAC  
AGGAGATGAGAAGCAAAATATATATTTCAACATCACACTCGTTGGGGGA  
ATTGACAGGATAGCAAACTGATTAAAGGAGGATAGGAGAGACTGAGATA  
TATATTTCCATATATATATATAGAGAGAGAGAGATATTTCCATATATA  
TATATAGATCTAGAGAGAGAGAGATAGAGAGAGAAGAGTCTTTCC  
>Contig51  
ACACATTTGGGGGAGCAGTTCCGGAGGTACAGCCCGGACAGGAGATGTGA  
GAAGATCGTGGTTANTGTTCCCTGGTCCAGAACCCCTCCAAGTGGGCTT  
AAGTAGGAAGGGTGGTGAGCGGCAGGTAAACACACGTCAAAGGCAGTCTT  
CCTCTCTGAGGGAAACACTTGTATAAGCATTGCAATCAATGGGCCTCTT  
TAATTATGTGCCAGTGGCAAGAGCGGGTGCTGAACCCAGGGGCCTGCCTC  
AATCCGGGGCCTTTGAGGCAGAATAAAGTGGTCTCAGGTTGTTGGCATT  
CCTTGCCCTTCCACCCGAAGCAGACACAAATCCTCTCTGGAGGCAAGTTC  
CCCAATTACGCCAGTACAACCTCCACAGACTAAGATCAATCATGTACAAG  
CTCACAGACAAAGGTCAACCAACACACAGAGCAATAAACAAATTCATGAG  
TGACGTGAATGAGAATAAACAGAAACAATAACCACAGCTGGGATGCTCT  
AAGTCTTCAGCTGTTAGAATTCCTGAATATAGAATAAACTGCCACAATG  
GCAAAACATGCATCTAGTACTTACTGTGTGCTGGGTTCTAAGAATTTTGCA  
CATTGTGCCAGATACCGACTCAGCTTCACACTCACCTCCTACTGTGCCC  
TCTTAATTTGCACTAGATTAAAAGGTAGAAAGGAAGAGGCAGCTATTCTG  
TTCTTGGCTGTGCCTCTGGCAGCATGCAAAATGGGCAGTAACAGTGGC

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AGTCACAGGTAAGTAGTCTCACAGCTGGAGTTAAAGGCATGGGAC  
GAGACGAGCAAGGTTCCATAAGGGACAGTGGCCAGTAAATGACCAGGGGC  
TACTGGAGTGGCTGCATGGCTCTGTGGAAGCTCAGAGGAGCCTTGGGTCC  
TGCAGGTGCAGTAGCAGCTTTCTGTAGTTCCTGATCTCTGGGTCCCACAA  
TCTTCCCCGTTTTTGTCTCCTCCACTTCTAATTTTGTAACTGACTTCCCTG  
TGTGTACTTCTCTCTCTGATTGAAATAGCCAGACTGGTTTCTGTTTCTG  
ATAAGACATTGTCTGGTACGAACACAGTAACATTTAATCCGATATCTC  
TATGAAGGAGGTACAATAATTATTCCTATTTTACAGATGAGGAAACACAG  
CAGAAAAATAAGTCAATTGTCTAAGGTTGCACATTTAGTCAAGGGAAGG  
GTTGATATAACATATAATTATTTAGAAAAACATCTAAGGAAATAAAAGGCA  
TAATTTAAAAATAAACTAGGCAGGTTTAAAAAATGAAGTAATCTATAA  
GTAAAAAGTATAATTGTTGAAATACATATCTTAGTGGATGGGTAAATA  
GCTGAAGAAATGATTAATGAACTGGAAGGTAGTTCTGAGGAAATCAGAAT  
TCAGCATAGATAGAAAAAATGGGAATTTACAAAAGTACACAGGAATTATA  
AAAGAGGTTAAATTATAGGGAGGGTAGAATGAGAATTAACATTGGTCTAA  
CTGGAATTTTGAAGAAGAGAATAGAGAGAATGAACAAGGCAATATTTAA  
AGAGGTGGCTGAGAATTTTTCAGAACCAACACAACTATGACTTTACCAG  
TAGAGAAAAAATGTACACTGAGGAGGATAAATAAATACTATGAACAA  
ATTGTAATAATAACTCAACAAAGACAAAGAGAAGATCTTAAATCAGC  
AAAAAAGAAAGTCAGACTTAGAAAGAAATGACAATGGCAGACTACTCAA  
CAACAACATGGAACCAAAATTCAGTGAAACAGTATTTTCAAAATGCATA  
TTTAATCTATCTTTGAAGAATAAGGGTGAAAAGGGTGAAAATTGCTGCCT  
TATACAAAATATCAACATTAACAAAAAGTAATGAAGGTAATATAAAATG  
TTTTCAATAAACAACAACTGAGAGAGTTTACCACCAACAAAGCATTCTTA  
AATGGACTTTTAAATGCAGTTTTTAGGAAGAAGGAAAAACAATTCCTAAGG  
AAGGTCTGAGATGCAAAAAGGAATTATGAACAAAGAAATGTTAAATTA  
TAGGTGAATTAAAAAAAGTGCCTGCATAAATGATAAATGACAATGATG  
CTATTAATAATGAGTTGATAAGGATAAAGAAAAAGGACAGAAATTAATAAC  
TAGAAAAACAAGCATGCTGGAAAGGATTGAGGAATTACTTGAAGGTTAAAG  
TTCTAGGGTCTTCTATCCTTCTAGAGGGGAGTCAATATATTAATTTTG  
ACCGTCACTTACACAGTGAAAAACTTTAAGGATAACCATAAAAAATAGA  
AATAGAGAGTATAACTTCTGAAACAGTCAAGGGAAAAATATGGAATAAGA  
AACTGACCAAAAAACATCTCAGTCAATCAAAAAAAAAAAAAAAAAAGAAA  
GAAAAGGTTCCGAAGGAGAAAAATCAAAGCATAGAAAAAGCGGGACAAATA  
GAAGTGAAAAAGAAAAAGGTAGAAGAAAAGGTCAGAAATATCACTGAT  
GCACTAAATCACCATTAAAGATGAAAACAATGAACAACATCAAAAAAT  
TCTAGTGAAGTGTAGTAGTGTGATCAGAATAGGCTCTAAGATAAGATGCA  
TTATTGTGAGTCAACTTGTGATGATGAAAGGTTAATTCACCAGAAAGAC  
ACAATTATAAACTTGTAAATCAATAGTTTTATTTTACTTTATTTAT  
TTATTTTTTTTGGAGACAGGATCTTGTCTGTGCTCAGGCTGGAGTGCAG  
TGGCTTGATCTCAGCTCACTGCAGCCTCCACCTCTTGAGGCTCAAGCTTT  
CTTCTGCCTTAGCCTCATGAGTAGCTGGGTCCACAGGCACACACCACCA  
AGCCCTGCTAATTTTTGTATTTTTGTAGAGATGGGGTTTCCCATGTTA  
CCAGGCTGGTCTCAAACTCTGGGCTCAAGCGATCTGCCCCCTCGGCTT  
CCCAAAGTGTTGGGATTATAGGCGTGAGCCACGGTGCCTGGCCTCAAATA  
ACTATTTAAGTGAACAAACTAGTATGGCCTAATGAAAAATGTATAAA  
TCCATAATCGCAGAGGGATTTCAACTTACTTCTTTCGATTATGTAAAGGT  
CAACAGACAAAAGACAATGACAAAATTAATGCAATGAACACTTTTGAT  
TTAATGAACATATATTGGATATGTACCAAGAATTAGAGAATACATACTA  
GTTTTGAGTTTATGCAGAACATTTACAAAAATTTAGTGGAAGCCTAAATT  
ATAAAAAGTTGCTGTACGTAGAATAACACACAAACCCCTGAGTCCGGAA  
TTCAAAGCCCTCCACACTCTCCTCTACCTTTGCATCTTTATCCTCCACCA  
CACTGCAGTGCATACTCTGGGCTACTACTCACTGTTCTTGATTCAAATTC  
CATGTTCTGTGAGCTCAATCATTCTCTGCTGGAATAACTACTTTCAT  
ACATATTCTGCTATTGAATCTTGTCTTAGCACCCCATCTACTCCAAGAC  
GATGTCCAGTTGGGGTTACTCCCTGTCCCATTTTCTTTGATTACACTTTT  
TTTTTCTACTTCCATTATATTATTGATCAGTGTGCCACAGTTTTTGA  
CTTTGTGTCTGCTTTTACTCTTTTCTAGACCCTGAGAGCTCCTGAAGGGT  
TGGGTCAATTTCTTTTATTTGCTCATTCTCATGGCACAGTGAGTGCTT  
AATAAATGGCTATTGACTGAAATTAACCTGTATCTAAATGGACATATTC

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ACTTCTGGGCCATTCACTTTCTTTCTATTGGAACCAGGAGATGGGAA  
CCATAACAAAGGTAAGGTTGTGCCATGTGAAAGAACATGGAACCTTCCCC  
TGAGGGCCAAAAAGAGCAGGGAAGGTGCAAAGACAAAATCTTCCATTT  
TTAAACAAATGTAAGAATGTGGTCCACCTCATGCTCAGGTGGGACTTTATC  
ATGACGTTATTTTTGGGGACTTATAGCTGCATCATTTACCCCATATACAT  
TTACCTTTAGTGTAGGGAAGTGAAGACAGGAATTTTGTGTGATGCAGACTC  
TTGCTAATGAGGCTAACACTTGGAGAAATTTTATCATGCATTCAAGAAGC  
TTGTTTACATTTCTTCATTAATACTTTAGTTGGTGGTTAGCTTTAGTT  
GTAGGCTTATCAGATATTTGGAGATATCTTCATAAACGATGGCTTTGGTT  
TTAGAAGAGTTATTCTGAAGCTACTATTTCTGGCAATAATCAAACAGCAT  
GGCCATTTGTTTTGTAAGGCCTTTCTAAAATATGACGGTAAAACTACG  
TGTGGAAAAATGCTTATTCTTCTGTCTCTATAAATGTGAATCTAGTTTG  
TCTTCAAATGAAATCAAGTGATTAATAATGTAGTTTTCTAAGAAGATAAA  
TGGAGCAAAGCACTCTGTGTTTACAGTGTTGGAAATCACTCATCCCTCA  
TAAACTGTCCCACTGATCCTGACTCACATGAATGAATTAATAAAGAG  
TTAATAACATCAATTTACATTTTTAAAGACACTTTCCCATGTTTTAGACT  
ATTGGTTGGAAAAGCTGGTAGGTGTACAATTTGTGGAGAGTTGGCTGTTT  
TTGTCTGTCTGTTGTTGACGTATTTCAAAGCCATATCTAATTTTGTGCA  
GAATGGTCTGAATTTCTACAAAATGTTGAGTTGTGTAGTGTGGAGAAGTA  
CGGAGCCATTTACTGAAAGGCTGGGGGGAAATGACGAGACCCTGAGATAA  
GGCAGTAGTGGTGGCAACAGAGTGAAGGGAGGTAGTTGAGATATGTTCA  
GAGTAGAATCAGAATGGACATAGTGAACAACTGGATGCAGGTGGGGCTG  
AGGAAGCAAAGTTGAGGATAATTCTGAGACTTCTAGGTTGATCCACTGAA  
GTTACATTTATTCAACACCACAAGGAACTAGGGGAATGAGAAGGCATACT  
GGTTTGCTTTGGAGTGAAGGGCAGTGATGTAAGAGGAGTTAATGAGTTA  
AAGTTTGGATATGCCTGAACCTTCAATTTGATATGTGCATCTGATATACCC  
TTGGGGTGACCCTCCAGGCAATGGTTGAACATGTGTATTTCTTAGTAAT  
GATAGGCATCACAGACTCACATCAGTAAGGAAGCAACAGCAAACCTTGATT  
GGACGATATACCTGGAACCTCAGTACCCTATGACTGGAGCAAGTCTCTGTC  
AGTGAAATGAGGATAAGAAGAATCTTGACCTTGTGGAATATGTTGTTAGG  
AATATATGTGATGAACAACATAGGATACTTCTACAGGGCTCCACATGTA  
GTAAGGGCTTTATAAATGCTTGATAAATATTATTGTTGTAATTTATTTCC  
AAAGTAAGATGCCACTGGAGGAATCTTTGGAACCCAAATTAATAACAAAT  
AGGACTGGATGCAATGGCTCACACCTGTAATCCAGCACTTTGGAAGGCC  
AAGGCAGGAGGATCTCTTGAGCCAGAAATTAAGACCAGCCTGGGTGAC  
ACAGGGAGACCTTGATCTATGAAGAATTAATAAATAAACCAGATGTG  
GTGGTGACGCCCTATAGTCCCTGCTGCTTGAGAGGCTGAGGTGGGAGGAT  
TGCTTGAGCCCATGAGGTTGAGGCTGCAGTGAGCCATAATTGTGCCACCA  
CACTCCAGACTGGGTGACAGAGTGAGACCCTATCTCAAATAAATAAATAA  
ATAAATAAATAAATAAGTACAAACCAGCAAACACTAATCCTTTCTAGAGA  
TTATTGAACTCTGGAGGGCAGATCTGAATGGAGCCAGCAGAGGGACCTAT  
GGAGATCAGCCTGGCCCTGGACAGCACCAGGCAATGGGGTTGCTAGAGAG  
GTAATGGGGTTGAACAGGGTTTAAGCCATGAGGTCTCAAGAATCCGTGAA  
GACTCAGACTAATTTTTTTTTTTTTCATGAGGATTAGGTGTTCCTAGGA  
ATTTCAATGAGAGCAGGGTTAATGAAGGAATGCAGGGTAGGAGAGCTGAG  
GGAAGGCATCTGAGAGAGCCTGGCTTATGAATGGCTGCGTCAGTATGGCT  
CACCTGCTTTCTTGATCTACTTAGCAGATGATCCACCCAGGCCTCC  
AGGGCCAAGGTCATTTCCACATAGTCATGGGCCCTTGAGGGCCTGGAGCA  
GTGTAAGGAAGACAGAGTCTTAAGAAATGCATTAACAGTCATGGTGCTT  
GGCAAGTGTCGTCATCCTATGCCAAGCCTGATCTGAAGGGGTGCATGCTC  
ATAGGTAGCTGCTGCCAAGATTACAGCAGCTTCTTCAATCCAGATCCA  
TGCTCTCCTATATTCAATTTTCCAGGGGTTCTGTCTTCGACAGTGATG  
AGATGCAGAATGACTTATTGAGTTATTCTCCTGATAGTTGCCAATTTTC  
CAAATGACAATGGGGCATGGAGCTTGAGAGTGGAAATGAGGCCCTAGGGA  
TAGCGTGCTTAGGAAAACACTCCAGCCTGATGTAATCTGGGGGTACAA  
TGGCATTTTCATCATCAAGACTGATGTAAAGGGTGAAGTAGCAGTGAGTTG  
GGGGTGACTCGCACTGGGGCTAGGTTTCTGATTCTGCCTAATCCAGACAG  
AGCAGAAGCACTAGTGGGCTGGTAGAGGGCCTCCAGGGCCTCACTTAATG  
TCCTGGAAAAACAGCTCCAGATTGTTGGTTTACGTTCTGAGGACAAGCTT  
GGGTACTACAGGATAGAGAGAGTGGTGGGAGATGCCGTGGCCTGCCCTGC

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TGATGCCTGCCCTGCCATTCTGCGTGTGATGTCTCTGGGGCATCTTGCC  
TTCCCTGCCCAGACCTGTAGTTTCTGAGGGCATGTGGAGGCCAAATGG  
CTTCTTAGAGTGTACTTTCTTGAACAGCTCTGCTGGGAGAACTGGAGG  
AGCTAGCTAGTCACGGTAAGTGCAGCAGTCAAAGGATCGTCCCGGTGGAG  
GTGGGGTGGAAAGGTAGAGAAAGAGAACATATAGCGTTTTCTTGGAGAT  
GTGTGGGCATGTCTAGAGGAAATACCCAATTCTGAGCCTTGAGCCCTC  
CAGGAAACCTTGGAATATTAGGTAGTCAATCCCAAGGAAGTCTAAGAAT  
TCTGGTCTCACCCATCTCTTTAATTCCCACAATGATCCTACATGATATT  
AAGGAACACGGGCCAGTAACCTCCAAGCAATGGATGTGGTGGTGAAGTT  
TGACCTCATGATGGAGCGGAGGTGGTTTGAACCTAAGAATTTAATTTA  
TTGTTTCAAACCTGTTCTCCACTCAGCGTTATTAAAGCATACATAATTGAC  
ACATAAAATTTGTATATGTCTACGGTGTACAATGTGATGTTTCGATCTAT  
GTATACATTGTGAAATGATTACAACAAGCTAAATAACATACCCATTATC  
GTGTTTCAAAGGAATTAAGTCAAGCACAAAAGAGAGGTGCTGTTGAAGA  
GTAGGGCTGCTCTATCTAAGTAGTATGTCTGGGGTGTCTGGATCAGGG  
TCCTTTTGTGCTAGTAATAAACAGCCCTTCTGGGGCTGCTCAGCTTCC  
CCACATTTTCTTCTGGAGCCTCCCTAAGAATTAGGACATGGCCACTTCT  
CTGCATAGGCTTCTTACTTCAACAGGACAGGGCTTGTGCTGCCCCATGC  
CACTTGAGTGTCCCTACAGCACAGAGCTGAGTGCACTGGCTGAGTGAG  
GAAATCCCCCAGATTAACTTGGTTCTAAGCATCATGGCTGTATTTACA  
CGTATATGAATTACAAATTACAGCATAGTCAATAAGGATTTTGTGCTA  
CAACTGGAATCCCAGATTATGCAAAATTGGATAGTATAATATTGAAATTC  
TAGGACTTTTATTAGTTTTAAAAAATTATACAAGCTTAGAGTAAGAAAT  
TAAACAGTGCAAAAGAAATCACTGTGAAAAGTAAATGCTCTGTCTCTGC  
TGAGAGACAGATATTGCAGCCAGATACTACTGGGGTCAATAGTTTCTT  
TAAGCATGCCATTTTGTATGGTTTATGGGACTTACAGCTCAAGAAGCTTGA  
CACTAGGGTTGATCTCAGAAAATCATTGTTGCAGGTATTAGATATGACCG  
TCTCATAAAGATACACACAGACACAGCGATTGGAGATATCACTGGGG  
CTTATGGGCTGCTTGTCTTTCTGCTCTGTGCTAAGTTGGGCTCAGAGT  
AGCCTGGCATCGGCTGTGGGAGAAATGCTGGCATGGGGTTAGCAGGAGCC  
CACTTAACATGTCTTAAGCCACCTGGAAGAGTCTTCAAGGAGACCAGAC  
TCCAGAGGCCCTAAGGAAGGAAGGACTTTTGGCCGTTTTTAGGTATTCTA  
GTCCCAGAGTTTAGGGAGGAATGGTTTGGCTTTGGGTCTGTGCCCCCTT  
ACCGAGTGGGATGGGATGTGCCCATGAGCTGTTGAGCTGGCTCTTGAGA  
AGACAGCAAAAGCGGGAATAAGAGGTGAGGAAGCTGTGTGGTTGTAGGAA  
ATCCCAGCAGAGGCCCTGGGGTCAAAAGTGGTCATGGTAGTGACGGTGG  
AGGCTGAGGTGGTAGAAAATCAGAGGACAAACCCCATGGGCTGCTGGTGA  
TCTGACCCAGCTCCTATGCTCTCTGTTTCAATTTAGGCTCTGTAGCAGC  
AGATGATTGGCTGGTGTGAGAGCAGTGCACCTGCCATATCAGGCAATCCA  
AGACAAGTCCAAGCTACGCTGGGAGGAAACCTGAAGGCAGCAGCAGGTAG  
ACTGGCTGAAGACAGACAGGCAGGCAACTTGTCAATCAGATTTGTGTTTT  
TAAGGACTTTTAACTGGGAGCCCTCCATGACAGATCAGATGAGAGAGGA  
ATCTGGGTCCGCCCATGTGTCAAGCTACCAGAGGGTCCCATCGGTGCTTG  
GATCTTCTTGAAGCTGGGTCTGAGGTTTGCAGGTAGAGGGTGAAGTGGT  
CAGAGGGACCTATTGCAGAGCTAACCACACCTTCCCAGGAATGCAAGCA  
CAAGCACCCACCGCGGGCAGGCGGGCAGGCACTTCTCTTTTGGCCCA  
GGACCTCACAGAGGCTGATCTGGCTCTGTGAGGTGGGAAAATGGGTTGTA  
CTTAGTACATAGAGATAAAAGGCTTAGGAGGCCCCCTCCATCCTGTGACCC  
TGTCCCCAGACCACAGGTGCCCGCAGGTGCTGCTATTTCAAGGCTGGGCC  
TCAGTGCAAGCTTGTGGTTTTCTTGGCCACCTGTGATGTCTCCACTAAT  
GAAGGGGCTCTCCATCTCTGTCTGCCTCTAGCAAGTGGAGGCTCTGGGC  
CCTGGGCAAGACACAGGGGGAAATGCCATCTGTTATCCAAATATATTTCA  
ATGTGACAGGAAAGCTGTCTTTAGAGCACAGC  
>Cont1952  
GCATGTGCTCTACATTGATCCCAGGAGTTTGAAGACAACATTGCAAGACTG  
GGCAACAAGCAAGACTCTGTCTCTACAAAAATAAAAAAATTAGTTGGG  
CATGGTGGTACATGCCTGTGGTCCCAGCTACTCTAAGTTGAAGAGGGAG  
AATTGCTTGAGGCCAGGAGTTCAAGGCTGCAGTGAGCTATGATCACACCA  
CTGCACTCTANCTGGGTGACAGAGCAAGACCCTGTCTCTAAAATAATAA  
TCGTAATACATTTTTTTTTAAAGTAAACAAAAAAGGTCACTTTCTCA

FIG. 4 (42 of 61)

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TACCAAAATAAATTCCAAATAAATTAAAGGCTTAAACATGAGAAAGTTAA  
ACCATAAAATTACTAGAAGAAAATAAAAGCAAATATTTAGATAATCCTGG  
GGATAAATTTCTTTGGAATGAATTCCTTAAGATGAATCTCTAAAAGTGA  
AATTCAGGGTTCAAAGGTCTTTCTTTGTCCTTTCTTTTCCCTTTCCCT  
CTCCCTTTTCTTTCTTTCTCTTTCTTTCTTTCTTTCTTTCTTTCT  
TTCTTTCTTTATCTTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT  
TGCTTGCTTGCTTTCTTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT  
TTCTCTTTCTTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT  
CTTCTTTCTTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT  
TTCTTTCTTTCTTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT  
TCTTTCTTTCTTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT  
TCTTTCTTTCTTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT  
AACAGTCGCATGAACATGGCTCACAGCAGCCTTGACCTCCTGGGTCAAG  
CAATTCTCCTGCCTCAGTCTCTCAAGTAGCTGAGACCACAGGCACCCACC  
ACCAAACCTGGCTAATTTTTGTATTTTAGTAGAGATGGGGTTTCACCAC  
ATTGGCCAGGCTGGTCTTGAACCTCCTGACCTCAGGTGATCTGCCTGCCTT  
GGCCTTCTGAAGTGCTGGGATTACAGGCTGGGCCTCTACGCGGGCCGAG  
ACTACCTCTCTTTAACTGGATCTCTGAGCTCTGGGCAGAGCCCACCCTG  
AATCCTGGTCTCCAAAAAGGGAATATTAGGAGGCTAGACCATATGAT  
GCTTTTACAGTGCACTTAAAAAAAGTTTGTTTTTTTTTTAAAGACATT  
TCTACATGTCTAACTACAATCTTCTTGAACCCCAAGAGTAGCTTCTG  
TTGCAATAGCTAGTCAAAATATAATAGTCAAAAAATCAGGTAAACAA  
CACAAACGCAAGCAGTTTAAAGAGCTGAAATGAACCTGTCTGTTTACACT  
TAGGGATTCCATAAGGAAAAATAGAAGTTTCTCCCTAAAAAGGGAGCCTGG  
CACCTTCTCCATTTTCTTTAAGGAACCCAGGCTATTATAAACTATTTTA  
GGGCTCTCATGCAGCAGACGGTGCAAGAGAAAGGAGAGACAGCAGAAGTA  
AATGAAGAAAAACAGAAATCCAGTCAACAGAGAAGAAAAAACTTTTGCTCA  
AAAAAAGGCAAGTTCTAGGAAAGAAAAAAACATGAGGGCTATTTAA  
ATACAAAGACGCATACATACATGCACACATCTTGGATGTTAGCTTTTA  
ATTAAGCTGACTTTTAACTATTGAGGTCCTTTAAAAATAAATCTTTTAAAA  
TCTTATTACGATATTTAGCTAGGACAAATTGCTGCTATTTTCAAGATTAC  
CAAGTATCAAAACCAGAAAGGCTTGATTTAGGAACCAACCCAGGCTGTC  
GTGGTAGGAAAAAAGGCAGAACGTTAGCTATGGAACCCACAGCATGGGGC  
AACAGCCATTGCTCTTTAGTATGGCCTGGCTAGCAAAAAGGTGGCCTTG  
TTATGTAAATAAAGCCCGTTTGGTGGTCAAAATGAAACATCTTTTCTTT  
TTTTTTTCTTTTGGTGGCCGTTTTTCCCCCACCATAACCAGTTTGTGT  
GTGTGGGAGGTTGGGAATTTAGCCACTTCAGAGGCTCATTCCCCATAAT  
TTGGAAATTTCTTTGGATTTGATCAAGTCAGATAGAGTAGGTCAAACCC  
AATGGGAAAAAGACTGAAACAGCAATAAAAAACAGAAACAAACAGTTAAGC  
AAAATGAATGATCACACAACCTTATATGATTACTGAGTGCTCTAATGGTAA  
GGAGAAATTAAGACCAGCTGGTTGTTAACTTTAGCCAAGACAAAACCCC  
AATTAGCTACTTACCTAGGGTTGGGTCTCAGGCTGAAGACCGCTCACTA  
CCGTTCTAGAAGCAAGAAATAAACTTGAACCTCGTCTTACCTGTGTAGCA  
GGACAAGCCGCAGACAAAATCCCTCAGACACCAAATTAAGAAGGAAGGG  
CTTTATTGGGCTGGAGCTGCGGCAAGACTCACGTCTCCAACACCGAGC  
TCCCCGAGTGTGCAATTCCTGTCCCTTTTAAGGGCTCACAACCTCTAAGGC  
GGTCCACATGAGAGAGTCGTGATAGATTGAGCAAGCAGGGGGTATGTGAC  
TGGGGCTGCATGCACCTGTAGTTAGAATGGAACAGAACATGACAGGGAT  
CTTCACAGTGCTTTTCTTATGCAAATAACCGATTAGATCAGGGGTGATC  
TTTACCAGGCCCAGGGTGTGTACCGGGCTGTCTGCTTGTGGATTTCAAT  
TCTGCCCTTTTAGTTATTACTTCTTTCTTTGGAGGCAGAAATTGGGCATAA  
GACAATATGAGGGTGGTCTCCTCTCTTACCTGCGGGGAGTGAGCTCAAA  
CTCCTTAAAGGAGTTACCTGCCTTCCATCATCAGGGAAGCAGGAAATCTT  
GCCTTCTTGTGGAAGCAAGTAAACTTCAAAACAAACAAAGAAAAAAC  
AGGGAGTTGTACAGCAAAATAAACTTTTGAATTTGACCAAATTTTGGGAG  
ATCAGGAATCTCTGAAGGAGATGCTTTCAGACCTCAGCAAATTTGTCTG  
TTGGTTTGAGCCATAAAGTTAGCTCATGCTGGTACCAAACACCAGTAGGA  
GATTTGTCAAAGGTAAGAGGCATCTCACTCAGAATCCCTTCGTGGTTAC  
CAACATGTGAACCTTGAAATCTGAGACAGGTCTCAGTTAATTTAGAAAG  
TTTATTTTGGCACGGTTGAGGACACCCACCCATGACAGAGCATCAGGAGG  
TCCTGACCACATGTGCTCAGGGTGGTCTGAGCACAGCTTGGTTTTACACA

FIG. 4 (43 of 61)

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TTT TAGGGAGACATGAGACATCAGTGAATATATGTAAGATGTACACTGGT  
TCCCTCCAGAAAGGCAGAACAACTTGAAGCAGGGAGGGAGCTTCCAGGTC  
ACAGGTAGGTGAGAGACAAACAATTGCATTCTTCTGAGTGTCTGATTAGC  
CTTTCCAAAGGAGGCAATCAGATATGCATTATCACAGTGAGCAGAGGGG  
TGACTTTGAATAGAATGGGAGGCAGGTTTGGCCTAAGCAGTTCCAGCTT  
GACTTTTCCCTTTAGCTTAGTGATTTGGAGGCCCAAGATTTATTTTCTT  
TCTACATCACTGTGGGCAGCTGACTAGGAAAGCTTTGTAGGACTGGTGGG  
CAGTGTGAGAGCCCAGTGGGGGGTGGTGGTCTGTGCCAATGGTAGCAAC  
CACCTGTGAGGCTGAGTAAACTCATTTCCTCAACCTCCTCTAGCAGCCCCA  
GTGGAGATACAGATGAAGCAGACTAGCGATACAACCCAGCCTGAAGTTTT  
GTCTGGTGAGTGTAATGGAATAAAAAATGGGAAGGGTGCTGAAGAGACCAG  
CAAGAAAATGGTTGAAGAGATGGGGCACAGAAATTAAGCTGGATCAAAAA  
GGACGGAAAAGCAGAAAGGGCCGATAGAGAGAGGGGATATCTATGGGTTC  
GCGATTCTGAAAAGGACAAATCACTGGTGTCTTTGAGAAGAGAGAGGGTGA  
GAAAGCAGGAAGGCTGGAGGCTGTCTCCAAGAGGCGGACATCTGTGAAC  
ATGATTTCAAGATCACCAGACCATGGGGGTGGCCAAAGGGAGTGCCTCT  
TCTCACCTCCTACTCTTAATTCCTTGTACTCAAGATAATAAGTTCCCGA  
AGAGAAGTACCCATATTTAATTCATCTGTGTCTTCTAGCAGTACTAAAA  
ATATTATATGAAAGGTATCAAACCTTTGAGAAATGTGTGCTGCTAAATTGT  
TAAGGATGCTGGAAAACCTCAAGACGTCCCTGATCCTGAGCCTGAGTATGA  
GCCTGTGGTGAGCCCAATGCAGGTCTCCATTGAGACAAAGGCCTCAGGGA  
ACGGATGAGACCTAGGGACAGAGATGCATGCTGGAGCAGCAATCCCCATC  
CCTACTGCAGCTCAGGCCAGCTGACTGCTTTATGAGTAAACGTTACCAGG  
GAACACTTTGCAGTCTTAACACACATGCCACCTGTGACCACTGATCCCT  
GTTGGGTGACCACTGACATCAGAGATTGATGGCAGCAATGAAGACAAGG  
CTATCCTCATTAGGAAGGAAAGGAAGGAGGAGGGAGGGGCAAAACGAAT  
CTTTCTGCTTGTCAACCACGTCCATCTCTGTAGGTGATTTCCCATGTG  
TGACTTTGTTTATCTTTATAATAACTCTGAGAGGTAGGTCTTGATGTCCA  
CATTTTGAACATGAGGACATCCAGCCAGGAAGTTGAGTTCTGGGGACATA  
GCTGAGAGGGCAAGCTACATATAAACCCCTCTTTGTTTTTTCTGGCTTA  
TCCACTGAGTGCCCCCTGCAATCCACAGCCCATTTGTGAAGTGCACTACT  
ATAGGTAAGTTGGCAAGGAGGAGTGGATGTGGGCGATTTGTGACAGCT  
CTCCAGGAACCTTACACACTGGTGAGGAGGGCCAGGTATGTTCTGACCAG  
TCACAATCAAAGCAACCTCCTACTAATCAGGGAGGCTTGGTACCTGGGGA  
ATGCTATGTTGAAAGGTTCTTTCTGGGTTTTAAATGATGGGTCTATTT  
CCTTATTCTTAAGATTGCTTTTTTTCTGGCTAGAACTTAAAGAAATTTT  
CAGTAAATTTCCCTTCCCTGGCACAAAGTGAGCTTGAAATGAATTCCCA  
GGTGGCCTTGATACTTTAAATATTTGCTCTATAAAATCAACCTTTAGA  
AGAAGGAAGTCAAAGAACATGCTAGATTTCAAAAGGTTAATTCCTTGAA  
ATCCAGTTATCTACAGGACAATGTTGTCAAAGAAAAAATTATTTGGCCAG  
GCACGGCGGCTCATGCCTATAATCCAGCACTTTGGGAGGCTGAGGCAGG  
TGGATCACCTGAGGTGAGGATTCGAGACCAGCCTGGCCAAACATGGTGAA  
ACCCCATCTCTACTAAAAATACAAAAAAATAGCCAGGTGTGGTGGTGG  
GCACCTGTAATCCAGCTACACGGGAGGCTGAGGCAGGAGAATCGCTTGA  
ACCCGGGAGGAGGAAGTTGCAGTGAGCCAAGTTCAAGCCACTGCACCCCA  
GCCTGGGCAACAGAGCAAGACTTTGTCTCAAAAAAAAAAAAAATTCAT  
GATATTTTTAAATTCATGGTAAGGAAGATTTCAATCAGAACAGCACAGA  
AGATATAGGAAACACTGCAATGGGACTTTGCGGTGGGGGAGAGAGATTGA  
ACACAACACTACATATACAGCACGGGCAAGGACATATTCATAGCCAGGAAGC  
AGAGCAAAGATCAGTGGATGCGAAATTACTAAGAGGAAACATGAAAAATA  
AGGGAGCTTCTGCCTAAACCCACCTAACCGGATCCTTGCTGAAGACAGGA  
CAGGGTGATTGGACACCACTTTGGGGATGGTGGAGGATGGGGAAATCCAGT  
GAGATTTCAAGGGTGATCAGATATTGAACATAGAAGGTTCTTGCTAAAAA  
AGGAGTTTACAAGAAAGTGTAACAATGTGCTGGGAGAAGGTTGAGGAGC  
CTGACTAAAAATTTGGTCAAGCAGAGAATATTTGCCAAGATAATAGCTAAG  
TCTTCTGACAAACAATAGATGCTAAGCCAGCAAGGGTGATGTGCTCAGAG  
AAAGCACTGAGGGCTTATTTCTTTTCCCCCAATCTCCACTCAGTCAAGT  
CTAGTCCCCTTGTCAATGTAGCCATTTGTAAGAATGCAATCAGGCAGGGT  
CCCATCTCCTAGTGACAGGACTGACTGAAGTTCTGCTGAAGAGAGTGGCC  
TGGGGCTGACACCGAGATTTAGAGTCTGGGTTTCGCCGAGAGCTCAGT

FIG. 4 (44 of 61)

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GTAGTGGCCATGCCCTCTCTCCACCTGAACGCCCAGTGTGGGCAGGAACAA  
CTGCAGCTAGAAGCTTGGCACTTACGCTGGGGTCTAAGACCTGCCTGATC  
TGCTAACTAGTCTTGTCCCTTGGCTATAAACTGACGTTGGCACCTGGCCA  
GAAAGATGAGCAAGAGATCTCTGACACACCTTTAAGTCCCTGTGGAGTAG  
GATTATGTTGGGAAGGTCACTTCTTGGACTGAGCAGCAATTTGAGAAGG  
AAGTCCCATGCCGAAGTGAGAGAAGGCAGGGAATCCTGCCTAGTCAGCTA  
GAGCAAAACAGTCTGCAGGACGGGACCCAGGGATGTGATCCTCCCATCCA  
AAGGCACTGAACTAAATGACTAAAATACTTTCCAGGGCTCACGTTCTTTG  
AAGAATGGGACTAAAACCTAAGACAGGAGCCAGCAAGTGAGGACTTGGAA  
GGAGATGGCTCATCTGATCAGCCTCCACTCAACAATTTTAATCATCCACA  
CTGGCATGGGGACACAATATGAATAAGTTGACAGGGACCTACTCTGATTA  
AGCAGTGGGCTAGTGCAGAGACCTGTCAGTCAAGAGTGGACAGGAGATGA  
TTTCAGACAGTGAGAACAAAATTAACAGAGTCATGTGCTAAAGGGTGGCT  
GGAACCTACAGAGGAGTTTAAGACTCAAGAGGTCTGGCTGGGCGCGGTGGC  
TCATGCCCTGTAATCCCAGCACTTTGGGAGGCCGAGGCGGGCGGATCACAA  
GGTGAGGAGATCAAGACCATCCTGGCTAACGCAAGTGAAACCGCATCTCTA  
CTAAAAATACAAAATATTAGCCAGGCGTGGTGGCGGGCACCTGTAGTCCC  
AGCTACTCGGGAGGCTGAGGCAAGAGAATGGCGTGAACCCGGGAGGCAGA  
GCTTGCAGTGAGCCAAGATTGCGCCACTGCCCTCCAGCCTGGGCGACAGA  
GCGAGACTCCGTCTCAAAAAAAAAAAAAAGACTTGAGGGAGTTGTTTTATT  
TTTGTCTCTTTTAAAGACAGGGTCTTTGTTGGGCGCGGTAGCTCACGCC  
TGTAAGTCCCAGCACTTTGGAAGGCTGAGGTGGAAGATCTCTTGAGCCCA  
GGAGTTTGAGGCCACTCTGGGCAACATAGCAAGACACCGTCTCTACAAAA  
AATGTGCAGGTTGAGGCTGCAGTGAGCAGAAAAACACCGCTGCCTCTAG  
CCTGGATGACAGAGCGAGACCTGTCTCGGAAAAAAAAAGAAAAAGACA  
GGGTCTCGCTGTGTACACAGGCTGGAATGCAATGGTGCAATCATGGTTC  
ACTACAGCCTGGAACCTCTGAGCTCAAGCAATTCCTTACCTTGGCCTAC  
CAAAGTTCTAGGACTACAGGTGTGAGCCACCACAGTGGCCTCAGGAGAG  
ATCTTAATAATAAAAGGACAAAATTGCCTTGATCCCTTAGGGGCAGGATT  
GACACTCAAGGATCAGGCAGAAAGCCTGTGCGGAGTGGGATGAGCAAA  
GAGAAAGGCTGAGAGTTGTGAAGAGGGAGATGCAGTGCCAGCTAGGACAG  
GCCTTTTTGGGCTATGGGAGGTTTTGAGAGGAGACCCACCTAAACTAAC  
CCATAACATTGCAGTGGGGACCTGTTGAAGTCATGGACTACTACCTGAAA  
GCCAGAGAAATGGGAGGAGCCTTCTCTGAGGAGGGAATCTAGTCCATA  
GGTATCTTGCCACCAAATACATGGACAGGCCCTGGGGGAAGATGGTGGTA  
GCCCAGCTGGAGGAAAAACCAATTTGCCACCTGAACTAGCCAGGGTAAGCC  
ACCCAGGCAGTGAAGGTGCACACCCATGCATGCACACACAGAATCACACT  
CCTTCTTATTATTCCTCAATTCAGGGGTCTCAACACCCATTTTTTTTGT  
TTTTGGGTTTTTTTTTACATGTTTTACATTTTATTTATTTATTTTGTGA  
CAGGGTCCCACTCTGTTGCCCAGGCTGGAGCACAGTGCAGTCGTGCAATC  
ATATTAGATTGGTGCAAAAGTAATCACGGTTTTTGTGATTAAAAGTTTTG  
CCATTACTTTTAAATGATAAAAAACCAGATTACTTTTGACGCAACTTAAAA  
GCTCACTGCAGCCTCAAAATTCCTGGTCTCAGGGAATCCTCCTGCCTCAG  
CTTCTGAATAGCTGGGACTACAGGCACATGCAATCCTACCTGGCTAATT  
TTTTAAAAATTTTTTTTTGTAAAGATAGAAAGTCATTTTGTGTCCAGGCT  
GGTTTTCAAACCTTTGTCTTTGTGCCTCCCTCTGCCCTGTGCAAGACCTTC  
TGGATGCCCACTAATGAAGACTTCCAGGGAGAGGAAAAAGTAAACATAGGT  
CCCTGATCAAGGGACAGGGTTTTATCGACCACAAACAGCATGCCAGATT  
CCACTGGCAGTCTTAGAGGTGCAATTTGCCCAAGTGTGTGTGGAAGGCC  
TCTCCCTAGCAGTTGGTTTTATACACCAGCCACAGCACAGCATATTCTCTT  
AAATTGTGAACATTTGCAAAAACCTCTGAGGACAACTATCATGTCTTGT  
GTACTTTTTGTTTTGTTTTCCCTTCCCCTATGTACACGCGCGCGCATGCACT  
CATGCACGCACGCGCGCGCGCACACACACACACACCCCTCAAACCTGAA  
TGCCTGGTGTGCTGAATGGATGAATGGCTAATGTAAGTCATTCTAAAAGC  
TACTTTCTTTGGCATAACCATCACCTTTGATTTTCTTTCTGGAACCTCCT  
ATGTTCCCAGATGAATTTGGAAGCCCTCAGGAAACATTTCAAATTTGCT  
ATATGGGAGAAATGGGAGGGTCTCTCTAGAAATTTACCTGCCACAGGTAT  
TTCTGGTAAGACACAGCAAAGGTGGCACCACCCATTCCTCGTTACAATGT  
CAATGCCAGTCACCTTCTGTCCCATAAAACCTTTATTAAAGGTGCAGAAAT  
TCCCATGGAAGCAGGTGGACACCATCTGCTTCCAGCCAGCCAGGGGAGCA

FIG. 4 (45 of 61)

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AGGTGTCCACTGTGCCCTTTGTGGCAGGAACCTGCGCTTCTCTACTCTCCCA  
CTTTGAGGCCTCTGGGGCTGGCCCTGCTCCTCATTGACAAAGGCTGCT  
TACTGAGCAGTTTCATTCTGAGCTGGACATAGTGCTTCTGGTGAGTCTCTA  
CTTCTATTTAAACCCAAAGATATTCTTTCTAAGGAAACGCTTTCTGTCTG  
GGGGAGGTTAGCTCCAGATGGAAGTCACAAGTGATGGCATGGTAGCTCTC  
ATCCGTTTGGGTGGATGATATTCACGGAGCACCACCATTGAGCCAGTCTATG  
GAGGTGAACAGTATATGCCAGCCCTGAATCAGGTGCATTGACAGCAAGGG  
AGACAAGCAAACAAAGCTGAGGTTTGTGAGGATGTTCAAGACTCACACA  
GCACAGAGGAGCATCCACCACCCAGCTTGGGAAAGGACTTGTGTATAGAGG  
GGGTGAAGCATGAGCTGAGTCTTGAAAGACTAGAAATTAGCCAAACTACA  
AGGAGGAGAAGGAGTTTCCAGTCAGGAAGAACAGGTTATGCAAAAGCACA  
GAGACTAGAAAGAATATCACATTCAGGAAGCTGCAAAATAGACAGGAAAGA  
TTGATGCGTGGGATAGGAGAGGAGGGGCAGGGGATTCCAGGTGGGCCCTGC  
TTGCCCACTCAGGAGCTTGAACCTATCCACAAAGGAGGTGTGGAACCGAG  
TAATGAATGGGTTTTGTGCAAGGCTTCATGTCACCGATTGCTTTTGTG  
GAGATACTTCTGTGGCTGATATGTGAGGAAGGGATGGAGGAATGTTCCGT  
GGCAATCAGGAAAACCAATTAGCAGATGATTCAAATGGCCTAGGGGAAAA  
GGGAGGAGGACTTGGACTACCATGCAGCAGCAGAAATGGAGAGAAATAAC  
AGATCCCAGGCACTCAGGAAGCGCTCAGAATGAGCCCTTCAAAGAACTTA  
TGGTAGGTGATGGATGGATGGAGTGTGAGTCTTGGGATAGCATTGCCTGG  
AAAAAFACTTTCTAGTTGAGACAGGGAAGTGGGCCAGCAGAAATGGAGGG  
CTTCTCTTTTTTGGCTTTAAATACTTTTATAATTTTGAACCTTTGAAAT  
GAGCAGATATATTAGCAAAAAGCCTAAAAGGGAATATTTTGAATCACTG  
CTAGTTCTAACATATAACTTTAGCTTGCACACATCATCAATTAACCTTG  
ATAGCGCCTTCTGAAACTATCATCCCAAATAGCAATCCTTGTA AAAACC  
TATTTTGA AAAACGGGCCTTG TAGGATAGCCTCACAGATGTTTGTGGTA  
GATTTTCTAACACTTAATGT CAGGGAGTGAAAGGAATCCCGTTAGAAGT  
TGGAAAATTTGGAATCTCTATTAGTATGATTAAGTTTTCGCGTCACAC  
AAAAGTTTAAACACCTTTACACAATCAGACTCTCTCATTTTACATTGCTCG  
GTAATTAGAGGAAATCAGTCACCCAGAGCCTGGGTCTAGACTTGACAAA  
ATGCACCCAAACAAATCCTGAGTGGCCTTGCTGAGGACTTCTCCAGAAGA  
TAGAAAACCTCAGTTCCAGCCAACAAGGGGGAAGCAGCTGAAGAAGTGAAA  
TTAACAAAGTCCTGGAAGGAAATGACCAAATCATCTTTGATTGTGTAATA  
ACCAGAGAGTAGAATAACAGTACGACATGAGTATTTTGGGAGAGAAGCATT  
TATCATAGCTTTTGAAGAGAATTTTTCAGCATCATAGCACACAATT  
CCAAGACAGATACTTTCAAGGGATTGTTTTGACG

>Cont1a53

ATGTTNNNGGTTTTGGGACCCCATTCAAACTTCATGTTGAATTTTAATCTT  
CAATGTTGAGCGAGGTCCTGTGGGAGGGTGATTTGGATCATGGGGTGGGT  
TCTCCCTTGCTGTTCTCAATGATAGTGAGTGAGTTCTCACAAGACCTGGT  
TATTTGAAAGTGTGTAGCACCTCTCCCCTTCATTCTCTCACTCGTCACTG  
CTCCGCCATAGTAAGATGTGTGTGTTTCCCCCTTGCCTTCCGCCATGATT  
GTAAGTTTCTGAAGCCTCCAGCTATGCTTCTCTGTACAGCCTGTAGAAC  
TGTGATTCAGTTAGACCTCTTTCTTCAAAATTACCCAGTCTCAGGTCA  
TTCTTTATAGCAGTGTGAGAGTGGATGAATATAGTGCCATATGTTGTAT  
TCCAGCTACCCAGGAGGCTGAGGTAAGAGGATTGCTTGTAGCCTGGGAGT  
TTAAGGCTGCAGTGAGCCATGACTGTACCACTGCTCTCCAGCCTGGGTGA  
CAGCGAGACCTTGTTTCAAAAAAAAAAAAAACCCAACTGTGTAAATGTG  
TTCATAAAAGTGTCTTGCTCCACACCTGTCCCTATATATCTTATTCCTC  
AGCCTCCGACAACACTCTTTATTCATTTCTTATGTATCTTCCAGAATCAAA  
AAAAAAAAATCAAATACAAGCAGTCAGTGAATGTATTGCCCTTCTTCCCT  
CCCTTTTGTTACATCAGATCAGATTAGCATATCAAAATACGTTCTGCATTTT  
TTCTTTTTTTCAGCTATCAGCATGTTTTTGAGAGGAAATTCATATTCTGTGCAG  
ACAGCATGTATTAGTCAGTCCTTGCATTGCTATAAGGAAATACCTGAGAC  
TGCATAATTTATAAAGAAAAGAGTTTAATTGGCTCACAGCTTCGCAGGC  
TGTTCCACAGGAAGCATGGCAGCATCTGCTTCTGGGGAGGCCTTAGGAAG  
CTTTTACTCATGCAGAAGACAAAAGCGGGAGTGGAATGTCTTATATGGCAGG  
AGCAGGACTGAGAGAGAGAGAGAGAGAGAGAAAGGATGCCACATCTTTT  
AAACAACCAGATCTTGTGGGAACTCTGTACAGGAAACAGCACCAAAAGGA  
TAGTGCTAAACCATTATAAGAACTCCACCCCCATGATCCAATCACCCCC

**FIG. 4 (46 of 61)**

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CACCAGGCCCCACCTCCAACATCGGGGATTACAATTTGACATGAGATTTG  
GGCTGGGACACAGAACCACCAATACCAGAGTGCTTTCTCATTCTTTTCT  
ATAGCTGCCTAGTATTCTATGTCCTTTACTTCATTTAGGCAGTCTCTTGT  
TGATAGACACTTGGGTTACTTCCAATTTTTCTATTACAAATGATGTGCA  
ATGAATAATTTTGATCATTTTCCATTTACATGGGTATGTCCATCTGTG  
GGATAAATCTCCAGGAGTGAAATTGCTGGATCAAAGGGGAAGTGCACTTG  
TGATTTTCATAGTTAGCAAATTTTGTCTATAAGGGTCATATCAATTTAT  
AGTCCCACGCGTAATATTTAACAGTGGGGATTTCCCGACAGTTTGACCAA  
CAAGGTCTGTGTAAACTTTTGATTTTGTCAATCTGATGGGAAAATAC  
TAGTATCTCAAAGTGCTTTTAATTTGACTTTCTTATTACAATGTAAAGCA  
TCATTTTACTCTGCCAAGATCAAATAGTATTTTCTTTTCTGTGAACAGA  
CTGTTAAGATCCCTTGCCCTCTTGTTTTGTCTGGATTTTGTCTTTTTTT  
CAAATGTTTTGAGGCAGTCTTTACATGTGAAACAAGTTATCTCTTTATC  
TGGGGTGTGAGTTACAACACTTTTCTCTGGCTTGTTTTGCCTTTTGAC  
TTTGCTTCTGGTGATTCCCGCAATTCTGAAAGTGACTTTTTCATCATT  
CATTCTTATACACCCATGCTCTTGTTCACGCTGGTTCTCTAECTGAGGG  
CTTTTTCTTTTCTTTTCTATCTGGGAACATTTTTTAGAGACAGGGTCTCA  
CTCTGTCTCCACGCTGGAGTGCAATGGTGCGATCACAGCTCACTGCAGT  
CTTGAACCTCTGGGCTCAAGCAATCCTCCAGTGTGAGCTTCCCAAGTAGC  
TAGGACTACAGGTGCATGCCAGCATGCCTGGCTGATTGTTTTATTATTT  
ATTTATTTTTGTAGAGATGGGAGTCTCAGTATGTTGCCAGGCTGGTCT  
TGAACCTCTGGGCTCAAGCGATCTTTCTGCCCCCTGCCACCCAAAGTGCTG  
GGATTACAGGCGTAAGCCACCATGCCAGCCCATGTGTGGAAATCTTCTG  
TTTATCCCTTTAGGCTTGATTCTTATGTGCTTCTCCTCCCTCCTTCTGG  
CTACTCCTCTTGTCTTTATCTTACTCTACTTGTGATGTTACCTTGTTTC  
TGCTTATAACTAGCTGCCTCTCCTATCTGAGGAGGGACTTGTGACTGTTT  
TCATCTCTGTACTCCAGGTCCTAGTACATAGCGCTTGCTCAACAGATGT  
TTGGTGCAATTGATAGATAAAATCAATGGTAGCTGTTAATACCAGTCTTGAC  
TCCCTGCAGTGCTTCAGCTGATCCTGTTCCAGATGTGCACTGAATATCTT  
TCTGTTGAACAACAGAAATAAAGGGGATGGGTGAGGAGGATAGTCTTCGG  
TGGCCAAGGATATTTGTAGGTACTTTGCAGCACTCAGCAATGAGGAGTGG  
GCTTTAGTCCCCCAAGAACTCTCACAGCCCTGTTTGTCTTTACTGTTTCA  
GTCAAATCCAAGACAAGTCAATGATCAGGAAAGACCTTTTTTTTTTCTTC  
AGTGAAGTTTATTTTCAAGACCAATTGAACAGTATGATATTTGCTCATTTAT  
AAATATTTCCCATTTAAATAATCTGAGCTTATATATTTTCAGTCTTAATTA  
AAGGACTTGATTTAAAGAGAGCACACCAGTCCAAATTGAATTGATTCCAT  
AGCTATTTAAAACTAGGCTCTTTTACAGACACTGCTACTTCTTGCCCCCT  
TTGAATAAATTAGACCAATGAATAAAACAAACAAATAAATAAATAA  
ATAGGGAAGCGGTTGCTCATCAGAAATGTGGGAGCGAATGACAGAGGGTTT  
CTTAGAACCAAAATGTGGCGTGTTTCTGTGAGGCGGGCTTTAAGTGAGT  
AGGAGAGGTGAGAGAGGCGCTGGCTCAACAAAAGGGCTGGGGATTGGCCCT  
GAAAGGAGAGAGCTGACTGTCTGGCTGATGGACAGGAGATCCTCTTAGC  
ACTACCTAAGGCAGGCAGTTGGGCATTGGTGTAGACAACAGGAAAGTCC  
AGGCTATAGCCGTACTCAAAAACCTTTCTGTTCCCTTTCTGCCAGCCCTA  
GGGATTGAGTCCACATTCAGCACAGGACTCTCTGGGTACAGCTCTCTTTA  
GGAAGACACAAATTGCATGGTGAAGTCAGTTATATCTGGCCGCTTTGG  
TCCCTCCCAGGAAGACGGGCATGTTTTCTGCTTGAGAGGTGCTGATGTAC  
CAGTTGGGGAAGTGGGCAGACTCAAATTCAGCTTGTATTGATTCTAT  
CTTGTTGAAGACAAATCGCTTTTCCATCTTCTTTGGGTAATTTTGG  
GATCTACACTCTGCAGCGAAAGAGAAAGAATTTTTGTGGGGCAAGGG  
ACAAAATGCTATGGGAAAGATGTTCTTTGGGTGGCCAGAAAGGAACT  
GACGAGCAGGTACATGATCAGGAGCCACACTCCTGAGTTGTAAGTGGC  
CCCCAACTTTCTGTGATTATTTAAAGAGCCCTCTTCTTTTCTAAAC  
TTAGTGCCAAATGCTGAGGAGCATAATGTAGGTGAGAATTTTTTTTTTT  
GGGGGGGTGAAAATTAAGCTAGAGCTTCTTGAAGTACCTAGTTTCCAGGG  
GCTTTTTATTGATTTTTTCTTATGGTCTTAGAATGACATCAACTTGGAA  
ATGAAGCTTTTGTGAGAAAGCTGGAGGTGATAGTGGTGGTGATTTTGGG  
AGTGGAGTGGACGTGATAATGGGACCCTTAAGTCATCTATTTCCCAAGG  
TGTCTATCAAATGAGAGCAGCCCTAACAAATATAATCTGTTGGGGTTGT  
AACTATGGTAGGACATAATAACATCGGCAAAATGATTTAATTTTCTGCAG

FIG. 4 (47 of 61)

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CAGGATTGAAGGTTGCAAGCAGTTAAAAATTATGTTAAATTTATTTACAT  
TAATGCAAAATTGTCAAATAGACCTGTTCCAGCTTTTCTAGGGATGGG  
GGCGGGGAGAAGGTGGTGTCTGGGAATAAGTGGTAGCAGGAGGCTGAGA  
AGGGCTTCATTCCATAGCATTCACTTACCTCCAGCTGTAGAGTGGGCTTA  
TCATCTTTCAACACGCGAGGACAGGTACAGATTCTTTTCTTGAGGCCAA  
GGCCACAGGTATTTTGTCACTTACTTTCTTCTCTGTACAAAGGACATGG  
AGAACACCACTGAAGAAAGAAGGGGGTCTTGTGGTTAGGGACACAGCAGT  
GCAGGGTCACCCCAACCCCTAGGCCCATGAGTAGGATACATGTAATTTG  
GTAGCCTCTGTGGGAACCCACAGTGAGGTTCTTGGCCTAAGACACAGGA  
TAACCTGACTTCTCACAGACAATAGCAGGGTCATTTTGTGATTTAGGGT  
TTCCCTCAAAGGCCTGAGGGTTTCTCAGAGCCTCATAGCAGTAGGAACG  
GAGAATGAAAGAGGGTCTACATTTTAAATGCTGAAGGAAGGAAGGAAGGA  
AGCCATTGTGTCACTGGCTGGCAATGTGCCCATCCACAGGAGCGGAACAA  
CTTGATCAATGTGGAAGGAAGGAAGAGGTGAGGCTGTACTTCTGCCAG  
AAATCAGGCACCAGAATGTTTTCAGGAACAGAGAGTAGCCCATGGGAAGA  
AACTGGGAGAGGAGAGGCTGAGCTGGGAAAGTGGCTCAAAGAGAGACAC  
TCATTTTGATCTTCTCAGTCAAGCAGTGTCATTTGGAAGGCCCTGGGA  
TCACTCTTACTACCCGATTTCAAAGAAAAGGATTTTCTTGGCCTGGCTG  
AGAGCAAAATAGCTTCCCTTGAAGTGGCTGTCTTCAAAGTCAGCAGC  
CTTAGTTGCCACACTCCTGTGCAGAGGCTTTGGCTACTGTGGCAGCATG  
CCAGGCAGATCACCACAGCTAATGATGGGTTACCGCACTTGAAACTTTT  
GCCCTTACAGCGGAGAGATATAAGTTCTGTGGCGGTAAAATTTCCC  
TACAAGGAACCACTGGCATTGGGTGGGACGGATGTTGGGGCAAGGGGG  
AAGACTGGGGAGGGGGATGGACACATTATCGCTCCAGCACTCTTGTTC  
GCCTCAACCAACAGGAAGAGAGAACCCACAGGCAGTTAGGCCATGTCCATC  
AAATGACCCCATATTGTGGAAGAATTGACATTGCACTATGCCCAAGAGAC  
TTGGGTGGACATGGTCTGGGAGTGCTTGAGCCGTCTAATTTCTCAGGGT  
CACACTCCTGTTAAACAAATGCACTGGCCAGTGCAATCAAAATGTGCCATTT  
CTAGGACCAAAGTTTGTATATTCTTTTAAATATTTTTCCTTGTGT  
TGATCATTTGCCCTTAAATTAATTTTCTACTTGTTTAAACATGGAGAAT  
TAGCAAGCTGCCAGGAAGCCAGGCAGGGAAACCAGGATGTTTCCATTTAC  
CTTGTGTCTCCATATCCTGTCCCTGGAGGTGGAGAGCTTTCAGTTTCATAT  
GGACCAGACATCACCAGCTTTTTTGTGTGAGTCCCGAGCGTGCAGTT  
CAGTGATCGTACAGGTGCATCGTGCACATAAGCCTCGTTATCCCATGTGT  
CGAAGAAGATAGGTTCTGAAATGTGGAGCACATGTTGTTTAGGTATAAAA  
TCAGAAGGGCAGGCCTCGTGAGGCAAGGTGGCAAAATTTGATTTCTTGGA  
GGACACCTGAGCATATACGGTCAAAGTCTGATGACAAACACCACTAGGGAT  
GAAGCTGGGAGTGGGGTGGCTAAGAACACTGGACCTGACACTATTAGACA  
TGGGTTCAGCTTTCAGGTCTATTACTGCTCACTGTGGCCGAGCAACAGAG  
CTACTTAGGTAAAATGGTGTATGGTCATAACACTAGCCACAGGGAGGTTA  
CGAACCTCTGGTGACAATGTAAGTGAAAGGCCCTGAGAAAGAGTGAGGG  
AGTTGCAAAATGTCAGTAGCCATCAAGATCTTCTTAAAGAAATAGTTTCCAC  
TAAAGAGATGATTGCTTTGGTTTCCAGCCTTCTTGTTTGTCTCCCCGC  
TGGGCCTTCTACCTTTAAAGGGCTTTGGCTCTGGGGGAATTGAGTTGGCT  
GGGGCTTGATGACTTCCAAGAGGACACAAGTGAGATCTACTGCCTGCTC  
TTGGCTAACTACCTTCTTCAAAGATGAAGGGAAAGAAGGTGCTCAGGTCA  
TTCTCCTGGAAGGTCTGTGGGCAGGGAACCAAGCATCTTCTCAGCTTGTC  
CATGGCCACAACACTGACGCGGCTGCCTGAAGCCCTTGCTGTAGTGGT  
GGTCGGAGATTCTAGCTGGATGCCGCCATCCAGAGGGCAGAGGTCCAGG  
TCCTGGAAGGAGCACTGCGGAGAGAGCGAGGGAGGGAGCCTGGTGAGGTG  
GTCCTGCCAGGAACCATGCTTTGACATCAGAGAGTAGAAAGCTCAGAGAG  
GAGGAAAGGCTTTGAAAGAATCCCGAGCTTCTAAAGATCATCCCTCTCTG  
GGCCAGGCGTGGTCTCATGCCTGTAAATCCAGCACTTTGGGAAGCCGA  
GGTGGATGAATCATTTAGGTCAGGACTTCAAACACAGCCTGGCCAAATG  
GCGAAACCCCTTCTCTACTAAAAATACAAAAATTAGCTGGGTGTGGTGGG  
GTGCACCTGTAATCCTAGCTATTGAGGAGACTGAGGAAGGAGAATCGCTT  
GAACCTCAGGAGGTGGAGGATGCAGTAAGCCAAGATTGTACCACTGCACTC  
CAGCCTGGGCAACAGAGTGAGACTCTGTCTCATAAAAACAAAAACAA  
AACAAAAACAAAAATAAAATAAAATAAAAGATTATCCCTCTCTGAA  
GCTCAAGGAGGTTAAGGGTGTACTCAAGGGCACACAGCAGGTTAGAGGCA

FIG. 4 (48 of 61)

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GA CTCAAGACTAGAAATG TGGGCTTTCTG CACCTTACAGGCTATTCTTTT  
AGAATAAAATCCCATTCTACTTTGTT CATCTTTTGTACATGCCCCACC  
TACACCATACATGTATACCTTCTCTATATCTTTTGTATCCCTAATGCTG  
TCACACTATGATTTGCTTTTTCATGCAGATGACCATAACATTTTCCATT  
ACCTATGCTCACTCAGCAAGTATTCAATTTTCTACACTGTTCTTTT  
TCCTTTTTCATAACACTGTCTCATAGGCATTCTGCAAATCCTGTGAGAGT  
ACTTTTGTGAAATGTTACCACTTCTCTTATTTCAGAGAAGCTCCGTAT  
TAAGGCTTCACTGAGGTTGCCTTAAGGCATGATAATGGTTCAAAGGCTTG  
AAAGACAGTTAAAGAGACCTGTAAGTGCACAAAAGAAAGTTGAGCAGGAG  
AGAATTTCTTGCTGGAGCAGAGCCAAGCTACTGGAAGAGGCAATGGGGG  
CAAAGGCCAGGCAGACAAGCCAATGGGCTCTCCACAGCTGCAGCCAAC  
AAGTTATGCCAGTCTTAAACTTCTAAAGAAATATGTTTTTAACAAGATT  
GAGGACTGGATTATGAGGCTAGGGGAGGCTATCACAACTGGAATAAAAT  
AAAGCCAGAGAAAAGTGGCTGCCTTCCAACCTGCACAACCTGACCTAGCTA  
GGCTGATGGCTGGGCCACCTAGGAAGGCTACTGAGCATCATATAAAACAG  
AAGGGACAGCAGGAATATAACATGGCTCTTTGTAAGGATGAGTCTGAAAA  
ATGACCACTTTGCTGCCCAAATGCCCTTAGCTACAACCTGAAAATATTTT  
AACTGGAGGTTG CAGGATGCTGGAATCTCAGAGATCATCCAGCTCAGCCC  
TTTATTTTTCAGATGAGGTCCAAAGCGGGTAAAATGACTTGTCAAGGTCA  
AACAGCAAGTGAATGGTTTTCTTTCAAGTCTCAATT CATCTTTTGTTTA  
TATCATCTATGCTTTGTTGTTATAAGCTTCAACCCAGGTAGCAAAAACT  
ATTCTACTCAAAAGGGGTAGACATATGTTAGTTCTCAAGATCATCTCTTG  
GTTTCAGAGTTTAACTCAAGTGATTGGCATAGGCTGAATCCATCTCTTAA  
AAGGATAATCAAATTTATGTTGAAGACTTGGTTGTCTTCTACTATGAAA  
TGGGAAACATTATCACTACTCTCTCCCTGTCAACCAAGTGTGGCCACC  
ACCACCAACGTTAGTGAGTGACTGTGGTGATATGATGACCAAGTGGCCAG  
GTCAGCAAGTGGTGCAGCCTGTGTCTCACTGGAAGAGGTTAAAGTCTTTC  
TAAACAAAATACCATGGCATCAAAGTGGCCCAGAACTCCCTTCTTTGAG  
CTTTCCTGTGTTAGAGCCCTTCTTGGGTTGGGAGTTAAACCCATAGTC  
TTACCTTCATCTGTTTAGGGCCATCAGCTTCAAAGAACAAGTCATCTCA  
TTGCCACTGTAATAAAAAACAGGGACATGTCTCAATTATGTCTTCTAAACA  
GGTTTATTTTCTTCTCTGTGTACAAGACTTGACTGTTTATAAGAACT  
GCAAACAGCCTGCCTCTCAAAGCTGCCTGAAACACCTGGCAAGTTTCACA  
GTGATATGCGCAGAACAGTCCAGAAGGCAGATTCTAGGCCTGGCAGGTGG  
GCACCCTGGGTGCTCCCTGTTGGATCTTGAGGCCTAACCTCTAGCCAGC  
AGAGTCAGCTAAAATCTGAGCTCTCCCTCTCCCTCCAAGCCACACTTTC  
AAAGGGATTCTTGTATTGTGGGCTTGGAAATCTTTTCTCCCATTTGCT  
CTGCAGGAAGCCCTTGCAACAACACATCTGGATAGCCTCCAGGTCCCAAG  
GCTGGAGGGACTTGTAATGGGAAAGTAGTCTTTAAATCAGATTTACTTGG  
CACCTGTGTTGCCACTGAAAGAGGCAATTTAGGGGAAAAATCTGGTCTCC  
AAGCACAGATAACACTCTACTCTTGAAGAGGAGACCTGCTCATGTTACT  
GGTCTCAGCGTCTCCACTGACCTGTAATAAGCCATCATTTCACTGGCGAG  
CTCAGGTACTTCTGCCATGGCTGCTTCAGACACCTGTGTAAAAAGGAGAA  
AATGAGTGACTTCCCCATGACGGCTACGTTTATGTGTGATTTCTCTCAGC  
ATCCAGTGCATGGCAGTCTATGCAAAGAAATGATCTCTGAGTAAATGAATG  
AATGTGTGAAAGAGAAGTCTTTGGGTCTAGAGAAAAGCATTGTCTAAAC  
CAAACCCCACTAGCAATGTATTGGCTAGGAGAGCTGGAGCAGAGGCTTT  
GACACTAACCTTTAGGGTGTGAGCTGTTAGATAAGCAGTATCCATTCCCA  
GAATATTTCCCGAGTCATAAGCATTATATTACACCTGGCATTTTTGCAAA  
AAGCTGAGAGAGGGAGGCAGAGAGGGAAGGAGAGGGAGAGACAGAGAAAG  
AAAGAGAGAGAGAGAGAGAATATGCATACACACAAAGAGGCAGAGAGACA  
GAGAGACTCCCTTAGCACCTAGTTGTAAGGAAGATTAAAGTCATACTTGA  
GCAATGAAGATTGGCTGAAGAGAATCCAGAGCAGCCTGTTGTGCCTTGT  
GCCTCGAAGAGGTTTGGTATCTGCCAGTTTCTCCCTCGCTGTTTTATAG  
CTTTCAAAGCAGAAGTAGGAGGCTGAGAAAATTTCTCTGTTGAATACCTG  
ATTTTCAATCAAGTTAAAGGAAAGGGGAAAAGAGTATGGTGGAAGCTT  
CTTAGGGGAGGGGACTAATAAACTGAGATAAATCTCTGGTTTATGGAAGG  
GCAAGGAGTAGCAAACTATGACACATTTTGCAAATGTATCACCATGCAAA  
TATGCATTGTTTTCTGACAATCGTTGTGCAGTTGATGTCCACATTAAAA  
TACTGGATTTTCCACGTTAGAAGAATGTTTAAATTTAGTATATGTGGGA

FIG. 4 (49 of 61)

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CAAAGTGGGAAGACACACAGATTTATACA.GCACATACTTTTCTTCATTCA  
CTTCTTTGTACTTAAGTTTtaggaATCTTCCCACTTACAGATGGATAAAATG  
GGTACAATGAAGGGCCAATAGCCCTCCCTGTCTGTATTGAGGGTGTGGGT  
CTCTACCTTGGGTGCTGTTCTCTGCCTCGGGAGCTCTCTGTCAATTGCAG  
GAGCCTCTGAGGAGAAAATTGACCTTTCTTGGCTGGGGCAGAGAACATAC  
GGTATGCAGGGTTCAGGCTCCTGACGGAGTTGGGGCAACCCTGGAGATAA  
GCTCACACAACCTGCAAGACCAGGTGCTGTTACCCTAGCCAATCTCATG  
GATGAACCAGATCAATGCCAGATGAGCTCTGCCTAAAATGATTTTTTGGT  
GAACTCTGAAAAGTGGAAATATTGTTTCTGTAAGAATATCCATCTGAGACT  
CTATCTCTTGGTAATACCAAGAGTTATCAGTTTCTCTTTAACCAGACAC  
CAGCAAAGTGCCTGCTCCAGGGTACTGCCAGGGGAGCCCTCCATTGTGA  
GAATGAATGAGAGTCCAGGTATGAACAGTGCCTGGAGTGTAGGAACACC  
CTCCTTTGCCTCTTTGACAGGTCTGCATCATAACACTTTTTTTTTTTTTT  
TGAGACAGAGTCTCACTCTGTGCCCCAGGCTGGAGTGCAGTGGCAGCATC  
TCGGCCCCCTGCAAGTTCCGCCTCCCGGGTTACACCATTCTCCTGCCTC  
AGCCTCCCCAGCAGCTGGGACTACAGGCACCTGCCGCCACGGCCGGCTAA  
TTTTTTGTATTTTAGTAGAGACAGGGTTTACCATGTTAGCCAGGATGG  
TCTCGATCTCCTGACCTTGTGATCTGCCCCGCTCGGCCTCCCAAAGTGTT  
GGGATTACAGGCGTGAGCCACCGTGTCCAGCCTGTAACACTTCTTATAGC  
ACTGAGTTGAAACCTTGCTCCTCCTGGTTCTCCAGGAAACTGAAATCTT  
TTTGAGCCAAGTCTAGCACAGTGCCTGGCATGTACATTGAGGTGGTAGAG  
TTTGCTGCTTGAATGGGTGAATGGGAATTTGACAGCATTTTTATTCAAAT  
TAGTATGTGCCAGGTATCGTGCTCGCTCTGCATTATCCAAGGGAGTGAGC  
CTCTGTGCAAGTATTTGAGACACGAGGGAAATAGGTTCTACTGTGGGAAA  
AAGAGCATTTCATGGACTTGCTCTCCAAGCAGCCTTCTGATTTTTAATTT  
GGCTCCCAGTATCTTGATATCAGGAGTCAGTACAGAAGTCCATCTTTA  
GTAAGTTATATTTCCACAGGAAATCTAAAAGCTGTTCAACATGTTAGTT  
TCCTGTGAATTTGATAAGCCATAATCCATTCTAACACTGAGCCCTCCTG  
AAATTTGGTGTCTGGTCTGCGATAGCTAAAAGCCCTGTCTGGGTGGCC  
TAGGGGACTCCTCTGTTTTGCCTCCACAGGATCCACTTTGCAAATTAACC  
ACTGGTCTCCCGTTGTAGGAACTGCCACCTTCTCAGAGCCTGTCTTTC  
TTCTTCTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTT  
TCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTT  
TCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTT  
TTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTT  
TTTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTT  
TTTGTCTCTCCCTCCCTTCTCTCTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTT  
CCTAGACAGGATCTACCTTTATCCCCAGGCTGGAGTGCAGTGGTACAAT  
CATGCATTCAATTGCATGATCACAGCAGCCTCAAACCCTTCTCAGAGTCT  
TTATGCGGCAACCAGCAGGGTCTGGAGGGTTGGTGGCTCTGTGAACCTC  
CTGACAGAACACAGAGATGTCTTTGGTCTGTTGATGTGATTACAAGCTGA  
ACGAAGGAGGATCAAAGCCAGTGAACGAAGGGAGATATGCAAGGGACCC  
GAGCATCAGCTCTGAGTTAGTCCATTCTGCTTCTGGGACTTGGGATACAG  
GTCAGAAACCTTGAGCTTCTACTTCTCCATCTTCCAATTGTAGCATCCAG  
GACCTCAGAACTTGCCAGCTAAGAGGAGCCCTAATGATTGTCTGGTGGGA  
TATGGTGGGACCACAGAGATGAAGACATGAATAGCTATTTGAATGTGAAC  
AGCAGACGAAGAAATCAAGGCTAGGAGGGTGGAAAGTGAATCATCCAATAG  
CACAGTGTGGTTGAAGCAGCACTAGTATCCAGGTTGCATGAGCCCTGAT  
GCTTTCCGCTCGAGGGAAATTTGGAGCCATGGGGCAATGCCCCCTGACGT  
AACAGTCTCCACAGTCTGCCATGTCTCATCCTGGCCCTGTAACCTGGAC  
CCAAATCTGCTACCATCCCATCCATCTCAGGAAGTGAAACCTCTTATGTC  
AAATAGGTTGTGCAACGTATGTATCAGATCCTGTCTTCCCAAGGAGACCG  
CTCAGGCCACAGCACTTCTTCCGATCCCCAATGAGCAGAAAATATCTCG  
CTATAACATAGTTGGCACTAAGGGAGGGAGTGGAAAGTGTATGATGATG  
TAGATGGTGTATGTAGCCCCAAGGAAGTGGAAACAAGCAGAGATGGGGAGCT  
GGAAATGCCAGGATGCTCCAGCTTTTGGGGAATTATTGAGCTCTTGAGTC  
ACTAAAGCCTTTCTCAGCTGCAAGTTCCTCTTTACCCTGTCAGGTCAATC  
TTCCAAGACAGGAGACTGACATTTATTCAAAGCAGCAAGTGCCCTGATAC  
CATCTTGTGTCTAATCATGGGCTTCGCAGCCAGTTATCAAGGTTGATCTC  
ATCTCATTTGGTCTTCAATCATTTTGAACAAGAAGACAAGCAAAATAATCA



TGGGTTAGTTCTTATATTATTGTGTGTACATGCAGTGATGTCTGTTCTTT  
GTAGTGAGCTGTTCTCTTCTGTTACCCTCTTGCTTAGAACAGAACTAA  
GCAATCTGCCCCAACATTTTCCCAATTTCCCATCTCATTCTTGGCACT  
GGCTTCTTAATATTTGTTCTTATGAGTCATTTTCTTGATCATTTCCATG  
AGTCCCTCTGGGATCTTAAAGTATGAAAAATGTTGTGTGTACCCACACCT  
GTCTTTGTGGATATTTCTCTCTTCTCCCTTCTGCTTCTGGGATTATTTGG  
GAATGGGCACTATGATTTTATCATATCGCTTCCACTTCTTTTATGGCAT  
CATCTCCAATGGGCTTCTCTCCCTCTTGGATCCAGGTTCTCAGATTGGG  
GACATGCAGAGTCCAAGGAACATTCCATTCTCTCCCTGGTCTAGAACAA  
GGAGGGCTTAGATATATGAGCAGGTGGCTGGGGCTGGCGAGCTATGTAGT  
CTCCAATGGCTTTTCCCTGATGTGGGAGTTGTTATGTCAGTTCTGGGAGA  
CCAATAAGACCTTGTCTTCTCTTGGATCCATCAGAAAAAGCCCCCTGGGT  
GGGTAAGATGGATGGCAGGGCTCTCCTACTCTATGTCTTTTCTCACACCT  
AGTGGGTATAAGAGAGGGGGACCACAAACAGAGGGGGCTCTGGTACCACTT  
ATCCAGGGTCTGGAAACATTTTCTGTAAAGGGCCAGATAATAAATGTTT  
AGGTACAACTACTCAACCTTGCATCATTTTCAGAAAAGCAGTCRGATAATA  
CATAAATGAATGGGTGTGGCTGGACTTGTCTGCGGTCCCCCTGTCTTATA  
TCATTGTATTATATCATTTTTTCTTACATACAAATTTAGAAGCAATACTT  
AAAAAAAAAAAAAGCCGCTCTTTATTGAGCACCTACTAAGTGCCAGGTACCT  
TTTTTCCCTCATTATCTTATTAACCTTTCATAATAACCTTTAAAGTAGA  
TAATATTGAACCATTTGACCTATGCAGAACTGAGGTTGAGACAATAAAT  
TATTTAAGACCGCACAAACAGTAAATGCTGGAACACGACTCAAATATGG  
GTTAACTGAACCAAAACAGATCTTTATTTCTCACTTTTAAATGTTACAT  
ATGTTTATTGCCTCATCTCCTGTCCACATGGTGCCCATCGGCAGACTCCT  
TTCTCATTCTCAGTGATTGAGTGACATTCTAACTACATTGGCCTGGCAG  
ATTCACCTCTGTCCCTAAATGTTTCCACATTGTCTTTTAGGATTGAGA  
TCCTCTCTGTTCCCTTGTCTTCCCTCCTTCTTCTTCTGGCGGTGACGTG  
CTGTGTGAATTTGTTTCTTCTCCTCTCAGGGTAGTACTGGGACTTTCCA  
AATCAGGGTTTTTAATGATCTCTCTCNCCTTTCTGAATTTCTTCTTAT  
TCCCATTCACTTTCTCATCTATAAGTGGCANCCTTTGTTGCTGGAAGATAT  
CCCTTGTGCAGGGATTNCTCTTTAANAATTTGTCNNNACC

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GTGATCGTCAACCTCCCACCCTGTAGGGCCTCAAGCATTGAGGACAATCA  
CTGGCTGCCCATTAAACCCAGAAATGTTGCCGAGACAGGAGGCCGTGGCCC  
AAGTTCTTGAATGGGGTATTATTATGTCAGCACAAAGGCCTTTGCACAA  
ATGAAGGCTTTAAAAATGCAGTCCTAGTCAGGTGGAGGAGGGCTTATAGG  
ATTCCCAGGAATCTGGATCATTCTCTTGAGAGCTTTCCCTTGTCTCTGTT  
AAAACTCACATCGTACGGCCCAAATAACAACAAAAATGGATGTAAATTC  
TTGAAATAACTTGTGGATGGGGGAACAAGGCCACCCCCCAGATCTGCCA  
GAAGCTTCAGGTGAGGGTCCCAAATGCCAAAAAGTCTGGTATCAGAGAGG  
ATGGCCAGTGACNTGGGGACACATGCCCTTTGCTGTGTCACTCAAGGAGC  
AGCAGCTTCGGCCCCCGCACAGTGACCAGGACCCTGGCTTCCCACGCTGGG  
CAGGAGCTGGTGTCTGATGAAGGGAATGCCTGGCAGCACGTGCTGTCTGT  
CTCCTCGTGTGAGCTTACCTGGCTTTGCTGCGAAGAGGCCACTTGCATTT  
CTTTATTTTTTATATTTTTTTTAAATTTTTTAAATTTTTTATTTTATTTTA  
TTTTTATTTATTTATTTATTTTAAATTTTTTTTAAATTTTTTAAATTATG  
CTTTAAGTTTTAGGGTACATGTGCACATTGTGCAGGTTAGTTACATACGC  
ATACATGCGCCATGCTGGTGCCTGCACCCACTAACTCGTCATCTAGCAT  
TAGGTATATCTCCAGGTTAATCCCTCCCCCCTCCCCCACCACCAAC  
AGTCCCAGAAATGTGATGTTCCCTTCTGTGTCCATGTGATCTCATTGA  
ATTTCTTTAAAGGTGGAATCTCTCAGTGGGTCTAATCTGTTTCAAGAAATA  
TCAAAAGAGTATCCTTGGGAATGACTGGAATTCAGAGTCATCTGGTAAT  
CCTCATAAAACAACCTCCTGGATGTCTCTCAGCACATCTCCACCTTGAAC  
GCAGGAGGCTGGTTCAAATGGAGGAGCATCGCTCTACTGCACTTTTTTTT  
TTTTTTGGCCTAAAGTGCAAAAGGGGATACGTTTCATGTAAATAAATCAA  
CTGCAAAATCGCTAGTTATGCTGAGCCCTGTCCCGTGTGTGGACACAAAG  
GAACCAAAAGGCTTTCTCCCCGCCAACACACACATAACACACACACAAA  
ATCATAAAAAACATACATACCCCCAACACATAACAACACACACACACA  
CAAAATATATACACACAACACACACCAACATGCCACAAACCTGTGTCC  
AAAAATAAATCCTACTGGTGGGTTTGTGGTCTCCCTAACTTCAAAATGA

FIG. 4 (51 of 61)

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AGCCGTGGACCTTCGCAAGTGAAGTGTACAGCTCTTAAAGATGGCATGGAT  
CCAAAGAGTGAAGCAGTAGCAACGTTTACTGTGAAGAGCAAAAGGACAAAG  
CTTCCACAACCCAGAAGGGGACCCAGCAGGGTTGCTGGTTGGGGTGGCC  
AGCTTTTACTTCCTTTTGGCCCTCCCATGTTCTGTTTCCATCCTATCAG  
AGTGCCCTTTTTTCAATCCTCCCTGTGATTGGCTACTTTTAGAATCCTGC  
TGATTGGTGCAATTTACAGAGTGCTGATTGGTGCGTTTTACAATCCCTT  
GTAAGACAGAAAAGTTCCCTGATTGGTGTGTTTTACAATCCTCTTGTAAGA  
CAGAAAAGTTCCCAAGTCCCACTGGACCCAGGAAGTCCACCTGGCCTC  
ACCTTTCAACTCCATAATGGCATGAAAATACATATGTTGTACAAAACATA  
CATACACAAAGTATACATGCATCTCCCAATATACACATACCACAGAAA  
CATACACACAGGAAGTCAAGTACCTGTCAAAAGTCTGCATGGTGATTGCC  
TCTGCAGTGAAGTAGTTAGAAAAGTGAATTTGTTTTCAATAAATTGGAGT  
CCTTAAAAATCGTTGTAAGATAGAAAATTTTTAAAAGTATATAAAATAAA  
ATAAGTATGTCTCTTGGTCTAGCATTTACACATGTAGGAATTTATCCTAG  
TGGAGTAATCAATGATATATGCAAAGATTTGGACAAGCATATTAAGCACA  
GAATTATGTATGCATATGTGTGTGTATATATATATATCTCATACATAT  
AATAATGTAAAAGTGAATAAATACTCAGATGTTCAAAATTGAGGATTAGTT  
AGACTATGATCTGTCCATATGTGACATACAAGTTAGCTGCCCTTATTCT  
CTCGAGCTTCAACCTCCTATAAACAGTGTCCCTTGTATATCAGTATTGGT  
ACAGATAATCGAAGCTTATTGAGGTTTTACATGGGGCAATAAAGGCAAGAG  
TTTATGAATACCTTACTACACTAGGTAGCACCCCTATTAAAGACAAA  
CTCTTCTCTCTCATTTCCCTTCTTTCCGGAACCACTTGGTTGAATCTCT  
ACAAGTCTCTATTGCAACTGCCTCAACATGGCACCCCTCCCTGCATCTCCA  
TCTTCCCTGTCTGAGAGCAATGGCCTGTGCCCCCACTCACATCTCTC  
ATTCAATCCAGAAGTGAAGCACCACAGAAGTGCCTACAGTTACCCCAACCA  
CCTTCTTAGAAGATAAGTTAGTGTGTTTGTGACTTTTTAAAATTTTAC  
TTCTCTTTTTCTTCAATCTCATCCCATCCCAAGAGGTTTATCAAGAA  
GTTCTCTAAAGATATGTGCTCTCTTATGGAATTTAACAGAAATCAGGGAT  
TTGTATTCTAGCCATCAAGGGAATAACATTTTTCCAGGTCTTTAGACAAA  
TAATGGAATACCTTGCAAGTAATTAGATACACTATTGTAGAAAAGTATTGA  
TGAAATGGAACGATGTTTGAGATATCATATTGAGTAGAAAAGGCAAGATA  
CATTAAAGTAGGAAATGTATCTTACAAAATAATTTGTGAGACACACTCCTA  
TATTTGTATGTTATATAAATGCGTATGTGAAGAAAGGCTAGAGGATGAGA  
CCACAGTCTCGGTGAAGTTTAAGAGATGAGGCTGCAGCATGCTCAGAAA  
GGCCTGGGTTATAGTTCTTCCAGTAATTAAGGATGTGATCTTGGGTAAAT  
TGTCCATCCTCTCTAACTGCACCACCTTTTGTCTGTAAAACAGGAAGGA  
TGGTATTTACCCCAAGGTCATCAAAGGATTTGGTTGGAGAAAAATAAAT  
AAATGGGCTGAGCCAGACCTGGCACAGTGAGAGCACAGTGGTTGACTAT  
TGTGCTGGCCTGTTGTTCTGTGTTATTGACATGCTGCTGGTGGTGGTCC  
AGAAGCTATTACCTTAATTGGTTATGTGGATTTCCCTCATACTGAGCAG  
CTGTGTGTGGTTGTGTAACATAGCCATACACAGTAAGTACAAGGGCA  
AATGTGATGGAAAAATGCAAGGAAGTGCAGATAAATAGCTAATGGGCTGT  
AGAAGGAAGCTAGTCTTGGAGGGCTTGATCAAGGAAGGTCTTTTGCAT  
GTCACCTTTGAAGAAGAGGGGACATAGAAGAGGTATAGTGCATCCCGGAG  
TGTACCTGGAAGGGAACATGAAAAGAGGACATTTTTCTCTGGGACATGGG  
GACTCCACTTGCATGAAGTCTGGAATTGGGGCAAAGAACCATCATGAGAA  
CAAGGGCTTCTTGAACCTCCAGGCTCATTGGCTGATCTAAACCTGTG  
TCCCCTCTTCTTCACTCTCTCTGTTTTCTATACCTGTATTATTGGAC  
TGGACTGGAAGCCACCTGATCTATCACAAGTACCTTGAAATGTGTTGAAT  
AGGTGTGGCACAGTCTTAGCAGAGTGGCACTACCCCAAGGAATTTGT  
TTATACCTTTGGCATGGAAAATAGCAGGAATGAGTGATCACTGATAACT  
GAGGATGCTATTTATTATTGGCCAAAGGAATACTTGTGTTGTATTGTCAT  
AACCCTCACAACTGTTGATTACAAATGAGTACCAGACCTAGCTCCTTC  
AAGTAAAGGATCTTGAGAACTGAAGGCAACAGAGCTCCAGGAGTCCAAG  
ACAGAGCCACAGACCAGGAGTCCCTGGCCAGGTAGGTGGTCTCTCTG  
CACTGGCTTTCAAGGCCAACAGGATGGATGGGGAAGTAGAGTAGCATCTG  
GCCATCTAGACCCTTGCTTTTTATCCCACTGGAAGCACATCTGAATTC  
TAAATATGATCTCTGAGACCTGCCAGAACCTTGCTCTCAGCCCCAGT  
AGCAGCCTGCTCTCTCCAGGAGGGCTTCACTAACAAGTAGGGCATTGC  
TGGAGGGCCAGGCAGACACTAGCTTAGGAAATCCACCAACCTTGGAATG

FIG. 4 (52 of 61)

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CTAGTCCCTTCTCTGAAGGCTCAGAAGACTGACTTTAGAGTCTAGAAAAAT  
ATTGGTCCTTGGGAACAGATTTTGGAGTCAAAGAGATGGACTTCAGATGG  
CCAGATGCACTGCTTCTTTAGGGAATTCTGTGAAAGCTCCCTGCATTTAT  
CTTAATACAGGCAGCAGATTTTCATGAGTACCCCCGAGGGATGGCCCCAGG  
TCCTCCAGCCTGTGAGCATCCTTCTGTCTTCAGCAGCACCACAGTATCT  
TTATATGTCTTTGGATACCTACGTTTCTGCCAGACATCTCTTGCTCTGAT  
GTTCTGGCTGCCAAATTCTCTGTCAAGCGCCTCCAATTTTTTGTGTCTT  
TGATTTACCCCCAATGACAAAGGCAGTTGTGCTTCATGTATTCAGGGAT  
ACTGCCAAACCACAAACAGGTTAAATCAAATAGCAGATATCCCTGTTCC  
TAAAGACCCATCAGCTCTACCCACCTGCTCCTGCTCACCCTCCTTATTGT  
TGAGTCTGAAGCCCTTCTTGTCTATTTTTATTTTTTGCATGAACAATTT  
AGTTCCCTTTGTCTCACTCCTAAACCTTTCTCAAAGGATTGGATTGTAC  
ACAAACTGCTTATCTCTGCAATCTTAGAAGTGATATGATTCTGAACAAAT  
CACTTAACTTTTGATTTTTTATTGGTAAGATGGGAATACCAATTTTTGCT  
CCACTCTGTCTATGTTGGCCTGGGCTGATGTTGAAAGCTCTCGGTCAA  
CTGAGATAGGGTGTGCAAGATTTATATATATAAATATATCTCTCCAACC  
CCTCCCAATGAAGCAAGTCACGTGAGTCAATCCTACCCTAAGATATTAGG  
GATTGAGCCTCCTGGGACATTTGGTGGCTTAGGTTTTCATGAAAAGAGGT  
TGCAGAGCAACTGCTTTTTGTTAGGCAAAGATTAGGCTACTGCAGAGACT  
CAGCAAACCTTCTATAGAAGGTGTGAGATGGTAAGTATTTTAGGCTTTGCT  
TGCCAGATGATCTCTCAACTAGTTAACCATGCTATTGTAGCCTCGAAGCA  
GCCAGAGACAATATGTAAACAAGAGCATGGCTGTGTTCAATAAAACTTT  
ATTTAAAAAACAGTCAGGGACCGGATTTGGCCAAAGGCCATAGTGTGCC  
AGCCCCAAGACTAGAGCAATGCACTTTTAACTTTTTTATTTTTTGT  
AAAATGCCAAGATCCACAAAAATGCTATTGCACCCCGTGTGTTAGCACTG  
TGACTCAAGGTTTGGGAAATTCTGCTTTGAAGGCGTGATAGACAGGAGAG  
CATGGTCTGGCCCCCTTGGTGCCTTTCTGGTTGCAGCGAGCATTTCAAAC  
ACAGAGCAAGGCCAGTGGTCTGTTCAAGCACTAGAGACATGCAGCAAGGTG  
TCCTGGGGTGAGAAGATGCCATAACTGGTCCCCCTTTCTATCTCCTTAGGT  
CTTGGACTTCATTCCATTTTCTGTTGAGTAATAAACTCAACGTTGAAAAT  
GTCCTTTGTGGGGGAGAACTCAGGAGTGAAAATGGGCTCTGAGGACTGGG  
AAAAAGATGAACCCAGTGCTGCTTAGAAGGTAAGGTTCTTGTAAGAAATC  
TACCTCAGGGCCAAAGTGTAATTCCTAGAGCAGAACTTTGCTAGGTGCTG  
TGCACAGACCCAGTTGTTTCTGCTGACTTGACAGTAAGTGAGCTTTCA  
AATTTCCCTGGACAAATAACTAGACAAGAGAAATTCGGAAGAGAAAAGG  
AAGCTTTGCTTCAGTGTCCAGGCACATCAGGTAGTAGATAAAAGGATCGT  
CCTCACCTACAGATTTGGGGCTTTAGCATCCTGTTTGCCAACTGGATGGT  
TGCAATGCTTCAAATGCACCTCTTCCCTCCCAACATTTCCCAAGTGGA  
GAGAAGCCTCCGATGAGAAGGAACTCTCTAAGGCTGGGCTGAACAAATGA  
CCCAGGCACAGGGCATCTGAGTATTCATGAGGAACACATTTGGGTGTTG  
CCCATGGGGGACAATAGGAGGAGGCTTTTGACCCAAATGATTGTCTACTG  
AGGTGTGACGGGAGAGGCTGTGACATGCCAGAGGCCAAACCCGTGATCC  
AGTTTCATCTCTATTCTATGTTTCTGAAGAGGGAAAGCTATGATTTAATGTC  
ATTACTATCATGCTGCTCTAGTATTTCTCAGCACATACAGAAAGAGGGA  
ATTAAATGGTCTTGATACCCCTAAATCCTTGGAAAATCCGAATTGCATA  
TGCTAACCTCACTGCGTCTGACTGCAGACCCGGCTGTAAGCCCCCTGGAA  
CCAGGCCCAAGCCTCCCCGCCATGAATTTTGTTCACACAAGTAAGGCCTC  
GGGGTGAGGTGATGGGGGTGGCTGAGGTGCGAGGGTGGGGATGGGGGATG  
GAGCCATTGGGTCTCTTACAGGGTGAGAGAATTGTAGAATGGGGACACC  
TAAGGGTGCTGGATGGGGCTGAAGTCTTTCTTTGTGGAAGCAAATCCCA  
TTAGGAGATAACTCTGGGAAAGATGAGCCCGGGGAGGGGCAGGTGATGCT  
CACCTGCTAAGAGGCAAAGGGCAAGGAAGAGTTTGTGCTGGGAACCTTC  
CAGGTGCTCTTCTGACCATAGCCAAAGAGACTGGAGACACAGACCTCCTC  
CCAGCACTGAGGACAAACAGCCATGGGGCCAGTGGGGGTGCAGGGACACC  
CACACCACTAAGGGCTCAGGGCGGCGCTTCAGAGCCTGAACCTTCTCT  
CATGCTGCCATTTGAACACCACAACACCCTAATAGGAACTGTTAATATT  
GCCACTGTTTCAAGGTGTGGAACCCGAGACAGACAGTGGAGATTCCCTGCCC  
TAGGTGACACAGGTAATAAGTGACAGATGTGGAATTTAAAGGTACTATA  
ACGTCTCTCTGCTGACTCAGGCTTAAGGCTCCCATCACCTCCTCTCTC  
AGGACAGAGTCAGGAGGCCTCAGCCTGAGCCCCAGCTCTAGTGCAGGTTT

FIG. 4 (53 of 61)

ATGTGGGAATACTGAGC. TCACTAGTAL. ATGGCAGAGAGGACCAAATGG  
GACCAGGTGTGTAAGGGTGCCTGGCACAGTTGGGGGAGGCTGCTGTGCT  
TCTCCACCGCTGCTGCTGCAGTTACCTTTGATGTTTTAGTTTTGTTGTAG  
TTACACCATTGCTGGCTTTGGATCTGCACTGTGTCCACTCCAGGTGGAAC  
CACGCACACAAGCCTCTCTGTGCGGCCTGTCTGACTTCTCCTTGTGAGG  
GCTGGGATCTCCTTCAAATCTGGCGGAAGTGGTTCTCCAAGTCTGGTCCT  
CAAACGTGACGAGCATCAGCGCCTAGAAGTGTAGGAATACACATTCCCA  
GGCCCCACCACAGACCTCCTGCCTCAGAACTCAGGGCGCTGAGGCTCTA  
GGGGCTGCTTTAAACAAGCCTTCCAGGTTATCGTGACGCACCTTGAAAGTC  
TGAGAGCTACTGCCCTACAGAAAGTTACTAGTGCCCTAAAGCTGGCGCTG  
GCACTGATGTTACTGCTGCTGTTGGAGTACAACCTCCCTATAGAAAACAA  
CTGCCAGCACCTTAAGACCACTCACACCTTCAGAGTGGCCTTGAGAAAGA  
TTTGGGGTCAAGGATCATGAGCGAGAACACCACTTAAGAGGATAGTGAAC  
TAGTCTGCATGTGAGACGCTGAGATCCTATGTGAGGCTGTGATAGGAGGG  
AAACAGAAAACCAAAGGAAAGAACAGCTTTAAGAAGCGCTTAAGAGGTACA  
AAGTAAAAATGATGGTGCTAGAAAAGTAGCTTCTTAAAAAGAGCATTTC  
AGTCTCACCTGGACTAATGAGAATCTCAGGAGTGTGAGGCCAG  
GTATCCATGGTCTTAAATGCCACCCACCAGGTGATTCCCAGTGTGCACC  
AGGGGTGAGAGTCACAGCCTTAGGCCATGCCACTCAAAGGGTGTCTTCAG  
ACCAGCAGCACCCACAGCTCTGGGAGTGCATCAGAAAGACAGAGGCTTGG  
CACCACCCACACCTACTGAACCATAGTTTGCAGGTGATTTCTTGACATT  
AAAGTGTGGGAAATGGAAAAGCTTAGAGTTGAGCTAGCTCGGTGACTCTC  
AGTCAACCTGCACCTGCTCCATGAACTCAGACTGCCTGGGATGGGCCAG  
AAAAGCTCCTGAGGAGATTCTGATGTAAGGCAGGGCTGATAACCATGGAT  
CTCATCTGACCCCATATCACTGGGGAGTTACTTAGGATCTTGCTGGGGC  
CAGTCATCTCTCCATAGACACTGAGAGTGTCCACGATGCTTGGGGCACT  
ACAGGGTGGGAGGTGGAGGATCACGGGTGAGTCAGATAGGAAGCCTGCTC  
CTGGGGAGCTTACAGTGCTATAGGGCAGCAAGCCAAGGATGCCAATACCT  
GTGTGCAGGTACCACTGACGAGTGCAGAGCGCTGCAGCACCAGAGAGGAA  
GCTACCCTGTGCAGAGGGGGCTGAGGAGGGCTGCAGGGAGATGACAGGAA  
AGCCGGTGTACAGGAGGAGTCTCCCCACTCTTTGGGCATGAGGAGACC  
AGGAGGACATTCTACAGTGAGAAACCCAGGCAGAGGCCATGTGCTTATGG  
CATGGGAAAAGAAATGACACCTTAGACTTATTCTCTACATTAGAAATGCCT  
ACCACAGATACCCATATTATAGCTTACATAGTGTGGTGGTTACTGTGTT  
TTCATATTGTACATTTGCCATTTTCCAGCCACCCACCCATTCTTGACAG  
TCACTGGCCCAGCCTGGGGGCCCTGTTCTTTATCAAACAAGTGCTGAG  
CTCTTTGACAGAGGTGAGGGTCACTGTCCAATCAGAGGCCAGGAGGGAAC  
GTTCCCTTTTAAGACCCTACTCTAGGCAGGCCTGGCCCAAATGAGTTGCT  
AGGAGCCCACGCCCTAAGAACCCTCTGAGCACTGTTGTGGCTGGTCTGCT  
TGCTAGAAAGTTGTTCTCCAGGGCCAGGTGCAAGATTTGTGGCTTTTCAA  
AGGAGCCCTAAAGCTCCAGCTCAGCCTTGACGGTGTGGGCTCCTGGG  
GGCTTCTGCTCCCAACCTCCCACTCTTCCATCACCGCTCCCTTAGCC  
TGGCCAGTGCAGGGATCTGTTCCACTCTAGGCACTGCTGAGGGAATGATG  
CCTCCAGTCAGAGGGTGCAAAAAAGAGAGTTAAGAAAAACAATGATTATA  
AAAAGTCTTTTTTATACGCCAGACATTTCTTTGCTCAGGCTAAGTGCTA  
CTTATTTGAGTAAGCATTTTAGTTCTCATAACTCCTCTCTCAAGTAGGTG  
CTGCTATTACTTTTCAATTCACAGATGAGGACATTGAGGTTTGGAGAGACT  
TAGTAACTTGTCTCTGTCTTACAGCAGAGCTGGGATTTGAATCTATCTG  
TCCAAATCTGGAACCCATTTGCTTGACAGAAAGCTTAATTGCTTGTCCC  
AGCAAGATAGAAAGCCTGGGAGTGGAAGAAATATTGAGTGGCTGTGATGT  
CTGAGCCCACAGGCAGGGTGGAGAGCTAGGGCTGGGGCCCTTGACGTGG  
GGAAGAAAGGGCTGAGTCTTCCATTTCAATGTGAAGTGTGATATCTGG  
TGATATTGATCTAGGTCCAAAGGTGAAGAACTTAAACCCGAAGAAATCA  
GCATTATGACCAGGATCAAAAGTACTGGTCTGGACTCTGGGAATCTC  
ATAGCAGTTCCAGATAAAAACTACATACGCCCAGGTGACTCTCAGTTTTG  
GCTGTGTTTTCTGCCTCCACCTAGCAGGGGTAAGGCCTCCTGCTAGGTGG  
GCTCAACTCCATGCTATACCATGCCCCATCTCCAGCAGGTGGTGGAGCG  
AGGAGGAGAGGGCCCCAGGGACTAGGGCATCAGATGAAGGGTCTCTAGCAA  
TGACCAGATCTGAAAGTAGTCTTTCTGGAAGGGCTGGAGAAAAAGAAGGA  
GGCAGACACTTAGACTGGAAGAAGAGGAGGCTTAAACCGGTGTGATGGAG

FIG. 4 (54 of 61)

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GGAGAAGTGGACCACAGAGTCAAGGGAGAGGGACTGTGCATCAGGCCTGA  
AACCCAGCAGACAGGAGAGACCTTCCCTGCTCTCAGAACCCACACATG  
TTCTGACTGTCTTTTTCCAGAGATCTTCTTTGCATTAGCCTCATCCTTGA  
GCTCAGCCTCTGCGGAGAAAGGAAGTCCGATTCTCCTGGGGGTCTCTAAA  
GGGGAGTTTTGTCTCTACTGTGACAAGGATAAAGGACAAAGTCATCCATC  
CCTTCAGCTGAAGGTGAGAGTTCTAGCTCAGTTTCTGGGCCTTTGGCTA  
CQCCAAAGTAAAGGCCAAGATCCTCAATGCCCTCTCGCTTTCCTGCAAAT  
TCTTATCTTGGCCAATATAACAGGGACATCCACCTTTCCTGGAAGCACCAG  
GCAGAAGAGCCCCATAACTTCTTCTCTGGTTCCTTGCCCCCTTCTAGGGAA  
GGAGGAGAGACTCCTCACAGCGGGGAGACAGCAAGGAGCTGAGCACCTGT  
TCTCCTCTCCTGGGCTCACTGGTCTGCGCCCTGGGCGGGTGGCGGTCCCC  
TCCTGCTGTGGCCCTCCATGTGGCAAGCAACACAATTGGGGCCAGGACCCT  
GGCGTGCTGTGTAGGGTAGGAGGGTGTGAGGGAGCACTCGGAGGGCAGT  
GTGTCTGCCCTGCAAATTTAGTCTGGATGGAGCATCCTTTCACTTGAGG  
GGAGAAATCTTAGGAAGCTGAATTAGATACAGATCTAAGCCATATTCTCT  
AATTTTAAAACTATAGAGCTGAGATTTTGGTATCCATCTGACTCTTACG  
TCTCTCTCTCTCTCTCTCTCTCTCAGTTTATTTTTAATCTGGGGACA  
AGAAGGCCTGGAAGAGAGGGCATGATTGCTTATCATCCCTTAAATACCAG  
TACCAAGGCTGACACGTCTCTTTCCCAAGGACCATCTGCCTTCTCTCTT  
TTCCCTCCTCTCCTGTGTAAAGGCCTGGAGGATGAGCACATGTGCTGTGT  
TTCCCTCCCTCTCAAAGCCTGTGCTATCTAATTAATCCCTTTTACCTCACA  
GAAGGAGAACTGATGAAGCTGGCTGCCCAAAGGAATCAGCACGCCCGGC  
CCTTCATCTTTTATAGGGCTCAGGTGGGCTCCTGGAACATGCTGGAGTCG  
GCGGCTCACCCCGGATGGTTCATCTGCACCTCCTGCAATTGTAATGAGCC  
TGTTGGGGTGACAGATAAATTTGAGAACAGGAAACACATTGAATTTTCAT  
TTCAACCAGTTTGCAAAGCTGAAATGAGCCCCAGTGAGGTGAGCGATTAG  
GAAACTGCCCCATTGAACGCCTTCTCGCTAATTTGAACTAATTGTATAA  
AAACACCAAACCTGCTCACTAACTTTCTGTCAATTGGGTTTCATTTCTCA  
TTCATGCTTTAAGGATTTGTGTTTTTATAGGATATAGCAAGAAGCTTGTTTA  
ATTACAAAGTTCTGGGTTGGAAAGAGACCGGCTTCTGCTTGTGTACTGCT  
ACCCTGAACCATCAGACATGCATGTGTGTGTATGCTATGATGTGGCC  
AGTCTGAGTGCAATACTTGCAGCGGGAAGGAGCAGCTGGGTGCATGCTGT  
GCTCTAGAATTAGTCTTTCTACTGGGGTTTGGTAGATTCTGAGGGCATT  
GATCCTGGGGCAGAAGTGGCTGAGTCTGTGTCTAGGGTACAGTGTGCAAG  
AAAGAAATGTAACAGCAAGTCAATCCAGCCAAGTGATAGTGGAAAAGG  
GGTAGTTAGTCCCAGATAAGGAGCAGGGTGACTTGACCTGTGGGAAAGG  
CACAGAGACAAGGAATCTGGGTGAGTGACAGCCAGGAGACCAGGTGAGG  
GAGGAGCCAGGTACTGTCTGGGAGGCTTGTCAACAAGGGCATGGTCTCTAT  
CACTAAGCAGGGCTCAGATCCTCATATGGGGGAGTGGAAGGCTGGCCGA  
ACAGAAATCAGGGCCTGGAAACAGAGTGAGGGGGTGGAGACAGGAGACTG  
AGGCTTGGAAATTAGTTTATTAGTTTTAGCTCTTCAGTTACAAGCAATAA  
TAATAGCTTCTAGCTTATTTAAGCAACAAGTATACTACAAAAGGAGCTTT  
CTAGAAGGATATTGGGTATATTCAATTTCTTACTGCTGCTGTAACAAATTA  
CCACCAACTTAGTGGTTTTAAACAATGCAATGTATTATCTTGCAATTATGG  
AGGTGAGTCTGGAATGTGTCTCACTGGGCCAAAATCAAAGTATCAGCAGG  
ATAGCATTGCTTTGGGAGGCTCTAGGGGAGAGTCAATTTCTTGCCTTTT  
CCAGCTTCCAGAGGCCACCTGCATTCTTGGCTAGTGGCCCACTCCCATC  
TTCGCTGCTTGGGTTTTTCTCACACTGCTTTGCTCTGACCCTCCTGCCTT  
CCTCTTTCACATATAAGAACGCTTGCAATTTACATCGGGCTCACGTCAAT  
ATCCAGGATACTCTCCCGTCTCAAAGAGGCTTAACCTTAAATCACAGATGC  
AAAGTCCCTTTTGCTATGTCTATGTAACATATACACAGGGTCTGGGGATTA  
GAATGTGGACATTTTCGGGGTGCCATTATTCTGCCTATCATGTGAAGTAA  
CTTTCAAAATGGAAAGACATGCTGAAGAAAAAGTCAGGGATTTCTGGCAG  
GCCAGAAATGACAGAAGGCAGAAAACGTTGGTCCCATCACTCAGATGGGT  
AAGAGCCAATCATGCTTTTTGTGAGTTAGCAAAAAGATTGAGATTCGAAGC  
AAAGCATGCAACTGCCCTAGTTTTGGGTGATGTGTGACTCCTTGGTCAGT  
GAAGGGCAGCACACCTTGATCAATACTCCCTCCAAGACTGTATCCAACGA  
GGCCAGTGATGTTCTCAAAGCAGAGCTAGAGAGCTAATCCCAGGAGAGA  
GGCGTGTGGGTGGTGGGCAGGAAGACAAAGCTCAGCCGTAAAGGAGTAGT  
AGGGACAGCACCTTAGGCATGGAGGCTCAAGTGAGATGATACCCATGGGA

FIG. 4 (55 of 61)

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AAAGCTCTGATAAGGTCAAGCTCCTTCTGTTTCTGATCCTGATGGTGATGG  
TGATCAACACCAGCCCAGTGACAAAAAAGTACATAGTATATTTAGTAGAT  
GTTTCCCACACAGAGAAATGGTAAATATTCAAGGCGAGGAATACTCCAAA  
CATCCTACCTTGATCATTACACATTCCGTGCATGTAATGAGTACTTGCAT  
GTATGCCATAAATATGTGAAATATTATGTATCACTATATAAAAGAAAAAA  
AAATGTGGCCAGGTGACATCCATATTTTGGAGAGGAAGGCATGTCTTCTT  
CATAATATCACAAAATATTTTCAACAACAAAGACACAGCTGTTCAAATTA  
GTCTCTGAGCCGGGGCTGTCTCATGGCAGTGAGGACTCTGGTTCCCTTAC  
AGACTAGCAGAAAGGAGATGGGGCTTACTGACCATGGCCTTGAGGAGGCT  
GAACATGCAGGCCAAATGGAGACACAGACAGCCTGGGCTTGGTCTGCTC  
CATCCCTTCCAACTGATGAGATATAGTGAGTCACTATGACGTGGGTCA  
CTCATGCTTCTGTGAGGCTCCACCAAGACAGCAAGTGCAACACCTT  
ACGGAAGCACAAAGGCCCTGTTTGTGTTGACTTCATGAAAGGCATGGTTG  
TGGTGATCGCATTGAGTAGGCTTTTGGGTGAGAGGTGAAAAACCCCACT  
ATCATGCATTGCAGCCCTCTGGTGGAAGCTGTGCTTCAGGCTCTAAATTT  
CAGGCTCTAGACTGACTCCAGGATGAGTATTTGGAAGCTGAAATCAATCT  
GTGGTCTCTTCTCCTGTAGAGCAGGAGTCAGCACTTTTCTAGAGTGCCA  
GATTCTATATATCCTGCCACATGCTCTGTTGTTACAGAACAAAGAAGGCC  
ATAGACAGCATGGCTGTGTTGGCAAATACACAAAACAGGCAATAAGCTGT  
ATTTGGCCTTTAGGCTGCAGTTTGCCAACCCCTGCACTAACACAGAGCTT  
AAAGGTGGTGGTGGTGTGCTGGAGCTAGCTTATATCAGCTTGCAATAGCC  
AATTGCTAACATCTCTTCCAACTCTGTGTCTGTGCCTTGATGTTGATAG  
TTTGAAATTGGCTACCCCATTTAATGCTGCAATCTTTTCTCACCCAGCA  
CTACTGACTCCCTTTGCCCTGTCTTATTTTCTCACTCTAACATGCTGT  
ATAGTTTCTTCTTACATTTATTGTTTGTGTCTTCCACTAGCATGTATGT  
CCCACAAGTTCCTTGTCTGTGATGTATCCCAAGAACCCACTGCAGTGCT  
TGGCACTTGTAAGAACTCCATAAGATTTTATAAATGAAGAAAGGAAGAA  
AAAAGAGAGGGAGGGAAAAAGGAAAGGAAGCCTTCTATTTAAATGATGGC  
CTTCTCCATATTTCTATAGTAATATGACTTCCCTTGCAAAGGGGGATGCA  
TTTTGGAAAAATGTGTATAAATAAACTCAGGTGGTTTTGAATTTCAATTTT  
CTAACTGTAATTGTAATCATTGGTCTTTATGTTTAGTGAAAAAGTTTTGG  
CCCTTATGCCTCACACCTGAGAATCCCAAAGTATTGGTTTGTAGAGCTC  
CCATAGAGAACCTCAAACTGGGTGGCTTAAACAAACAGAAATGTATCGTC  
TCCTGGTTCCAGGAGGCCAAAGTCTGAACTCCAGGTGTTGGTTCAATCTGA  
GAGCTCTGAGAGAGAATCTGTTCCAGGCTTCCCTTCAGTTTGTGGTAGCT  
CCAGGGTTCCTTGGCTGGTGGCAGCAAACTCCAGTCTCTGCCCCATCT  
TCAGATGACTGTCTTCTCTGTGTTTCTGTGTCCAGATTGTCTTATAAG  
GACAGAGTCATACTGAATTAGGGCTCACTCGAATGACTTCATCTTAAGTT  
GAACTGTATCTGTAAAGACCTTATTTCCAAGTAAGGTCACATTACAGCT  
ACTGGGGATAGGACCTCAACATATCTTTTGGGGGACATAATTCAACTC  
ATAATACCCAACATGATAACTGTTTCACTCCCATGAAATTTAATGTCTCTCA  
AAAGGTGATCTCAGGGCATTAACTCTGTGACAGAACTCCCATAGGAAAC  
ATTCCAACCAGAAGCTCCTTTCACAGCTGGTCACTCCTCCTACCCCATCC  
GAGGTCTGGGGCAGGGTGAGGCAGGTGGGGACAAGAAGGCTGTCTC  
GGGTGTAGAAAGAGAAGACCCTTATTCACCCGGCACTCTGTTTATGAATG  
AGCTATCCAGCATAGGATATAATAAATCGCTTTAGGAGTGGTAGACTCCA  
AACATTTTTTTGGTCCAGTTATCCTAATCAATTAAACAAACTCTAGAAC  
CCATCTTGAAGTGCAGGCATTGGGACATTATGAAACTTACACAGAATTCA  
AAAATTTACAAGGGCTAAATAAAAACAGGGTCTGACATCTAATATTTTCTT  
CCCACATTCCCATGCACTGTCTGGCTCAACCATCCCCAACCTCACTCTC  
ATCCTGGTGGACACATGCCTAGTGATGTGATCAGCTGGTTACAGGGGGC  
TGGTGATGGTGGATATACAGCTTTTGCCAAATTTCCATGGCATAACTACTC  
CAAATATGGCCAATTTCAAACCTACCAACATGAAGGCACAGACACAGAGTT  
TGGAAGAGATGTTTAGCAATTGGCTATTGCAAGCTGATATAAGCTAGCTCC  
AGCACAGACACCACCGCTACCTTTAAGCTCCTTGTGTTAGTGCAAGGGTTG  
GCAAACCTGCAGCCTAAAGGCCAAATACAGCTTACTGCCTGTTTTGTGTAT  
TTGCCAACACAGCCATGCTGTCTATGGCCTTCTTTGTTCTGTAACAACAG  
AGCATGTGGCAGGATATATAGAATCTGGCAGTCTTTAATAAGTGCTGACT  
CCTGCTCTACAGGAGAACACAGATTGTCTTCAGCTTCCAAACATTCTCT  
CTGAGTCAGTCTAGAGCCTGAAATTTAGACTGAAGCACAGTTTTCCACCAG

FIG. 4 (56 of 61)

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AGGGCTGCAATGCATGALAGTTGGGGTTTTACCTCTCACCCAAAAGCCT  
ACTCAATTTTTACTGCAAAAACATGTTATCATCATTATTTTTACTTAG  
CCCACCTTTCCTTGGCAATTTCCATAGGAAAATGCATTCTAAATTTCAA  
CTAATCAGGGGACTTGGAGCCTCTGGACACCCCTTGTCTTGCCACA  
GTCCCTTGCGAGAAGGTGCCTTATCAGAGCGGCTCCATGCAGGGGCTCAGG  
ACAGGATCAGATGTCAGTTGCACCAAGGGGCGAGGACAGATCCTCTCTG  
CTEACCATGCAGAAGGGACTGTTCAGTGCACCGTCATGGTCTGTGATT  
TCTGGTCCATAAGGGAATTTTCACATGCATCGGGTGATTGTCACATCAGC  
ACAACACTGTGAGGAAGGCAGAGTGAGAAATTTGTGTGCCATTTTATAGG  
TGAGAAAACAGATGCAGAGACATTAAGTAACTTCACCACAGTCATGCGGG  
TTTTAAGTGGCAGACTTTCAGGTGTTGTGACTCCTAGTCCAGAGTCTTT  
GCACTGCCCCCTGAGGTGCTAAAACCTCTACTGTGCTTTAAGACTCACTTGG  
GGAGCTTCTTAAAAAGAGAGATTGCACAACCTGAGATTCTTGTTTAACTG  
TTTTGGGATGTAGCTCAGGGATCTAGCTGCCTTAAAAAATAAACTCCCA  
AGTAATTTCTGATGCAAGCGGTTCTTTTTGTCCACCTTTGAAGAAACACT  
GCCTCCTCCCCATACATTTTATTAGAAAATGGTAACATGTTTTCAGCCT  
GAGAGCCATTTCTGGGTGACCGGACGTGCGCAGCCCGCTGTACTAGCTTT  
CAGTCTAGGCTTAAACACACATGATAGGAGATGTCCTACTCCAGATGATA  
TGAGTCTGAACCATGGAAAATTCATTGTGTGGCACATCTGGTGGGTGT  
GCACTGTCCCCAGCAGTGAGGCACCCAGTGAAGACAGCAGCTGGGAGAGG  
CTTAGTTACATGCAGTGGGACAGTGTGGGCTAGACTGCTGAGCCCTCTGC  
AGTTTACTCTGTGTGAGGCAATGAGGGTGAAAGGCTGATCAGACCCAGT  
GCAGACCATACCCTCCAGGGAGACAGATATCAGTCAGGACAACCCCAAGT  
GTAGCTGGAGAAGCAGTGCCAGGTATGACCGGATGTGTATCCAACAGG  
AAATCTGCATATAAATATAAGAGGAGAAAATGAACAGATGTTGCTCTTAT  
ATGTAGATATTTATGAAGAGCATATAATTTTGTGTTTGTGTGTTTAAAGAA  
GTTTATAAGTATGCCTTAAAAATGTATAGTATATACTGTAGGTATTTTT  
CCATTAGATATTTTTGTTTTTCTACTTATCCACATTGACATTGTAGCAAC  
AGTATAATATAACAACCTCCTCTACAAAAGCAGAAGGAAGTGAAGCTTTG  
GAAGGAAGCACCAGTGAGCTTGCCCTTTGAGGTGGGTGCAGTGAGCAG  
GAGTCAGTGAGGTGAGATCCTTTGAGAGGAGGCAATCATTAAACCAGGAA  
ATCTGCATGCATCCTGGCCACACCTAACCTTGGACAATGGTGCTTGGA  
GCGCCTTCCAGCTCTTAAGGCTTGCGATTTCTTTCTCTCACTCTTCAACC  
ACGATGATTAAATCTTCTCTACAGAGTTGGACAATAAAGCCTTGAGTTC  
CTGCCTCCCCCTGGTGTGATCACGAGGCATAGACATGGCCAGGAACATGTA  
GGTGTCTTTGAAAGCTGAACAAGTTAGTAAATTTCAAACCTCATTTCACC  
CACCAGTAAATGGGAATAATAATAAACCTATTTTACATAGGGTTGACAA  
GAGGAGTAAAGAGGGATTCAATGAAAGTTCGTTATTATCATTGTAGTAG  
CAGTGTGATAATATCAACTGAAAGTTCATTATCATTATTAGTAGCAGTA  
TTGATAACCCCTCTTTCTGTGCCTTCTCACTGGTGGGCCCAGGCCATCAG  
CAATGCCCAGGGTGTGATGGATCTCTGCTGCATCGGGCACCAGCTGTGTC  
AATGGTGAGAACAGTACAAGGGTGGGCAGGGCAAGGCAGGAAGCACCAG  
GAGCAGCAGCTTCATGGGGTGAAGATGTCAGGAGCTTAGGGACAGTCAGA  
GCGGGTGTGCCTCCTCTTGTGGAGCCTTCTGCGTGGGTAGGAACTGCTG  
CAGCTGTGGCCATGGATTACCTGAATATGGGTGGAATTAGGCATTCAGC  
TGGGTTAGCTGTGCCTAGAAGGAGGAACTCTAACTGAGAACTGTCCCT  
ATTGCCACCTCTGATAGGCAGATGATCCATCCATCAGTGGCTGAGCTGAG  
GTGTGCATGGGGATGGGTAAGAGCCACACACAGGGCTGATGACTGAGTC  
TATTTAGAACAATAGATGTAAATCTGATAATGTAAATGTGATAGATTA  
TTTGTCAATTAGAAATGGTACCATATAATTATATATATACATAAACATG  
TATACATATACACATATACATGTGTGTATAAACACACACAGTATTGTC  
CCCTACTCATCCATAAACCTGATGCCCTTAGCTGGGATTCCAGCTTTC  
ACTCTCCTCTCTGTCTGCTGTCTATATCCTCCCCATCCTGTAATTCT  
GGCTTATATGCCACTTCTCCTAAAGCCCTCCCTCAATCCCTTGCTGGA  
AGTGACATTTTCTCTTTGAGCTGCCCCCTGCTTGTGCTTTGGTGAGGTCA  
GCTGTATTGCAGTACCTTGTATTGTGGTTGTACATCATCGTATAGAATT  
AATTTCTGACACATTCCGTATTTTTCAAAGGGCCTAGTGTGGGGCTTTAA  
CAGTAACTACGCCACCACGCCAGTTAATTTTTGTATTTTTGGTGAGGA  
CAAGGTTTCACCATGTTGGCCGGGCTGGTTTCGAACTCCTGACTTCAGGT  
GATCTGTCTGCCTCAGCCTCCTGGAGTGCTAGGATTGCAGGCATGAGCCA

FIG. 4 (57 of 61)

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CTGCACCCAGCCACCTATCAAAAATTTAAGTGCCATTTTATTTTATT  
TTTTGTAGAAATGGACAAGCTGATCGCAAAATTCACATGGAATTGCAGGA  
GGTTCCAAATAGCCAAAACAATCTTGAAAAAGAAGAACAAAGTTGGAGGA  
TTTACACTTTCCAGTTTCAAGACTTAGCTCTTAGCTACAAAGCTACAGTA  
ATCAGAACACTATGGTCCTGGCATAAGTGATGCTGGACAGGTGAGCCCCA  
AAGTGGGACTTAACCTGTGAAGGTTCTTGGCCTTGCCCAGGAAGGAATTC  
AAGGGCAAGCCAATGGGACAAGAAAACAGCTTTATTGAAGGGGCAGTATT  
ACAGCTCCAGCCCTGTTACAGCTCCAGCCCTGTTACAACCTCTGACTACTC  
CTGCACAGAAGGGCTACCCCTGTAGGCAGAGAGTAGCAACTCAGGGCAGTT  
TTGCAGTCATTTATATCCACTTTTAACACATGCAGATTAAGGGACAATTT  
ATGCAGAAATTTCTACGGAATTGGTAATAACTTTTGGGTGATGGAGTCAT  
CATGGAAGGGGGCGGGAACTCCCTGGTGTGGCATGATGACGGTAAAC  
TGATATGGCGAACTGGTGGGTATGTCACATGAAAAGCTCCTTCCACCCCA  
GCCCTGTTTCAATTAGTCCTCGGTTTGGTCCAGTGTCCAAGTCTGCCTC  
CAGAGTCAAGTCCCACCCCTACCTCTTAAGGAGAGATGTAAATACATGG  
AATAGAATTGAGAGTCCAGAAATAATCTCATACATCTATGATCAATTGAT  
TTTCAGCAAAGGTGCCAAGACCATTCAATGAGGGAAAGAATCATATTTT  
TTCAACAAATGGTGTCTGGATAACCACATGTGAAAGAATGCAACTGGGCC  
TTATCTCACACCATATACAGAAATTAACCTCAAAATGGCTCAAACACTTAC  
ATGTAAGAGCTAAAACATAATATTCTTAGAAGAAAACAGGGATATATCT  
TTATGACCTTGGATTTGCTGGCTGATTCTTAAATGACACTGAAAGCACA  
GCAACAAAAGAAAAAATAGGTAAATTGGACCTCATCAAAATTTAAAA  
CTTTTATGCTGGGTGCACACCTGTAATCCCAGCACTTTGGGAGGCTGAGG  
CAGGAGGATCTCTTGAGCCCAAGAAGCTGAGGCTACAGTGAGCCGAAAT  
GTGCCACTGCACCTCAGCCTGGGTGACAGAGCAAGACCTGTCTCGAATA  
AATAAATAAACAAATATATAATTATAGATCTCTGGATCTTGCCTTCGGAG  
ACTGACTCAACTAACTGGTCTGGGTGGGAGCCCAGCCATTTGTATTTTT  
GAAAACCTCTCAAATGATTTTACTGTGCAGCCAAGGTTGAGAATCACTGT  
ATCATAGGGTTGGACTCCTAACTGGAAACAGTTTGCACCATCAGGTGTCTG  
CAGCATTCTGATAATAGTTAAGCTTTCTCCTAGATTTTCTGATATTAGA  
TGAGTCATGTTTACAAGTTTTTACCAAGAGACAAACTATCTTTCTGCCCT  
TACTTTCTCTTATACTATTCTAATCCCAGAACCCTTTGGAACCTTCCAC  
TGAGAGATGAATCTAGAAAAGTGACTCTCTTGGCTACAACAGAGAGTAATG  
TTGGCCTGTTTGTGCCAGATCCAGTTGGTGTCTGGTGGTGGGACAGCACCT  
CCCTGAAATCCCCTCCTCTCCCGTCAGATTCAGTCCCCCATTTGCATCAC  
GTACAATCATCACTATGGGTTTCTATTACCTTGCTAGGGCATTTGGAGGT  
ACCATATATACCAACTATTAGTTTTGAGCCATGGTTCCCAAAGTGTGGAC  
TGAGGGGCACCTCAGCACACTCAGAGGTGTCTGAGGATATTTAAATATT  
CTGAAGAAAACACAGTGACATCTGTGAGGCCCCGTGAAAACCGTTGGCATT  
AAATTGTCTCAACCCAATTGCTTAAAGAGCAGAACTGGCCAGGCACGGTG  
GCTCACATCTGTAATCCAGCACTTTGGGAGGCCGAGGCCGGCAGATCAC  
GAGGTCAGGAGTTGAGACCAGCCTGACCAACATAGTGAAAACCCCGTCTC  
TACTAAAAATATAAAAATTAGCCATGCATGGTGGCATGCACCTGTAACCC  
CAGCTACTCAGGAGGCTGAGGCAGGAGAAATGCTTGAACCTGGGAAGCGG  
AGGTTGTAGTGAGCCAAAATCGTGCCACTGCACTCCAGCTTGGGTGATAG  
TGAGACTACATCTCAAAAAAAAAAAAAATGAGAGAGAGAGAGAGAAGCAGA  
ACCATCAGGTGTTTCTTTTGGCTTAAAGTACTCTGTGAAGAAATTCCTGG  
GACACGAAGGATACCATGAACTGAGAGATTTGGGAACCTCTGCTTTAGA  
AGCTGGAGGTAGCATTCTTGGGCACAGTACTGCCTTGGGATCAGCAAT  
CCTTTTGTGGTGCATTTAGGTGTGGCAAGACAGCTCTTAGAGTGGGACC  
GGGATGTGCTTGGAGACAGAGGGAAGTAGATTGAGCTGCCCGATAAAGAC  
ATGCCAGCCTGGCAGAGTGTAGTACTCATGTCTGTAATCCTAGTGCTTT  
GGGAGGCTGAAGTGGGAGGATTGCTTGAAGGCCAGGGGTTTGAATCAGCC  
TGGGAAACAACAAGACCTCTACAAAAAAAAAAGAAAAAAAAAATTAACCA  
CATGTGGTGGCATGCACCTGTAGTCCCAGCTACCTGGCAGGCTGAGGTAG  
GAGGATCACTTGAGCCCAGGAAGGTAAGGATACATTGAGCCATGACTGTG  
CCACTGCACTCTAGCCTGGGTGACAGAAAGAGACTCTGTCTCAGAAATAA  
ATTAATAATAATAATAATATATAGTGGCCATGACATCCCTAGAAAGACA  
AGGTCCTGGGAATAGGTAGAAGCCAAGGGAAATGAGAAATGAGAGGGGGC  
CCTGGAGCTGGAACCTGGGGGAGCAGGATGGCCTCTGAGAAGTTCTTGATA

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GTGGTGTCACTGATGTGTCTGATGTTTAGTTGTAATTATTTGCTGGGCCC  
CTGTCACTCCCTCATATCTGATAGCTCTTTGCTAGTCAAAGTGTGGTCTGG  
GGATCAGCGGCATCAGCATCACTTGAGAACTTGTTAGAGATGCAGAATCT  
AGAGCCCCACCCGGGACCCAGAAACAGAGCCTGCATTTTAAACAAGCTCCC  
CAGGTGATTTCTCACACACACTCGCATTTGAGAAGCACTGGGCTAGTTGAC  
AGATTCTCAGGCATGGCTGACATTGAAATATCCAGGGAGCAGGCTTGGCA  
TTAGGATGTTTTAAAAGTCTCTCAGGTGTTTCTAAAGCCAGGTTTGAGGAA  
TTACTGGGCTGATACAAATGTTTTGTGATGATGCTTTGTGTGTGTGTGTG  
TG  
TGGGTCACTTGGCACCAACACAGGAAACAATGGAAATATGTGAGCCATGA  
CAGAAAGGTCAAGGAGATAAAAGAAATTAGTGACATGAGAGGTACTCCTCA  
GGTGTTAGGAAAGAGGGTAGAGCAAAACCAGGTTTTCCACCATATGTTGGA  
TAGGGGGTCAAGTAAATTTCTACTTAAAAATTACAAACAGGGGCTGGGCG  
CGGTGGCTCATGCTGTAAATCCCGCACTTTGGGAGGCTGAGGAGGGCGGA  
TCACAAGGTCAAGAGATTGAGACCATCCTGGCCAACACGGTGAAACCGTG  
TCTCCACTAAAAATACAAAAATTAGCTGGGCATGGTGGTGCCTGCTTTA  
TTCCAGCTACTCGGGAGGCTGAGGCAGGAGAATCGCTTGAACCTGGGAG  
GTGGAGGTTGCAGTGGGCCGAGATCGCACCACTGCAATCCAGAGCGAGAC  
TGTGTCAAAAAAAAAAAAAAAAAAGAAAAATCCAAACAGGATGACCTAAG  
CCTGCAGGACTTGGAGACATCTAGGTGACTGATACTCAGTCACAAAACAT  
AATTGGTCACAGGCCTGATGAAATGCACAGCAGACCTTCAGATGGTATGC  
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TTGGCATCAATCTCTATCAACAAAGATAGTCCAAAGCAATGGGTCCAA  
AAACACTTTCTAAGACAAATTCTCTATTTGCTTTTAAATATCAGTCATCC  
CAGCCCTTGGAATAGAGGAGCAAATGATACCAGTGGTACCCTACCACAT  
GCACCAAGGTATATATCTCTCATGCTCCATTTTCTCCCTCTGTCTACATC  
ACTAATAACTCATTGATTTCTGGTGCAAGCCCTGCTGGGAGAAAAAGTCT  
ACTCTTGACCTTGGAGCAAGTTGCTCAGAGTAGGTATCGAGGATAAAAT  
TTGGAAAGTTAGAAAAGCTATTAGAAGGAGATCCTAGTAGTTGAAAACAC  
AGCCTGGCCAAGTCAATGATGCTATTTCTCTCCCGCCTTGCTGTGCTCC  
ATAGCTAAGGAAGACAATTTAGGCTTGGGCTAGAGGATGGGAAAGGGCAA  
AATTACTGATGCCACAGCCAGAGAGGTATTTAGTAATCTGAGGGTGAG  
GACCACATACCTGGTTTCAAGGACGTACAGTGTGACAGCTGTGAGTGGAT  
GCCTGGAGTTCTGGCGTGTCTTCTAGCACAAATGATACCTGAGACTCTTGC  
ATCATTTGGGAATAATAAAATGGGAGTGGATAGATATGAAATTATGATGGC  
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GCAAATCCTTTGGTCCAGGTTTGGGATATAGGCAGCATTGTATTGGAAT  
GCTGATAGTCTGAGGCCATGAAAAGTCCACCTGCAGTAGTGGTAGGAGGA  
ACAAGCCTCACTTTCTTCAATGTGTGTGACTGCTGTCTTGATTCCCTGGG  
TGGCCAGTTCCATTTCGTGTGGTTCTTTGGTCCACTTGACTCTGGGGTGGC  
TCTGTGATGGCTTGACCAATACAATGTAGTGGAAATGATGCTGTGCATCAT  
TTCCAGCCTCTTCCAGCCTTAAGGAACTGGCACTTTTATTTCTGTCCCT  
TGGAAATCTTGTCTTGCAACCCATCCATCATACTGAGAAATTCTAAG  
CTGCCCCATTAAGAGGCCACATGGTGATAAATTGGGGTCTTACATACAG  
CCCTAGCTGTGCTCCTAGCTGACAAACAGTAGCAACTTGTCAACAGCGA  
GTGAACCACTTAGGACTGTATACTCCAGCCCCAGTTGAGCAATGTGGAAC  
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AAATAATCCCTAGGCTTTGGGCTGATTGTTCCAGATTACTGGAACAGA  
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ACTTTTAGGGAGGGTTGAAGCATAGTGAGGAAAACAGTAGGGGAAGCTAG  
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CCTGATGTAATGTGGGAAATTGTAAGAACTCAGAACGATTTAAGGGCATG  
TTTTATAGGTCCTTTAAGAACTTCTAGGCCAGGCGCAGTGGCTCATGTC  
TGTAATCCCAGCACTTTGGGAGGCTGAGGTGGGCGGATCACAAGGTGAGG  
AGATCGAGACAATCCTGGCTAACATTGTGAAACCCCGTCTCTACTAAAC  
TACAAAAAAATTAGCCGGCATGGTGGCGGGTGCCTGTAGTCCAGCT  
ACTAGGGAGGCTGAGGCAGAAGATGGCGTGAACCTGGGATGTGGATCTT  
GAAGTGAGCCAGATTGTGCCACTGCACTCCAGCCTGGGCAACAGAGTGA  
GACTCCGTCTCAACCCGAAAAAAAAAAAAAAAAAGAACTTCTAGGGC

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TGGTCCCGTGGAAGCCTCACACATGGTACACAAAGGCTGTCTTGAAAAGA  
AACGTAAGTGTGTTTTTGGTTTAAATAAAATTGATTATAAATGGATAATG  
CAAAACATTTTAAAGAATTTTACTAGCTTACATTAGCAGATTTGGATCCA  
GTGATTGTTACATTCTGGTACTGAGCCCCTGAATTACTTCTTTGAGTAAG  
GCATTATACCAAAGCTATTGATAGTTGGGCTTATAGGGTGTATGTTTGAA  
GAAGTACTAATGTCAAAACCAATATTTTACGGTTCGACAAGAGGACATCAG  
AACTGGTAATCCTTATTACCATGACTGGCTGGACAGAATACTCAATGTAA  
TGGGATTTCTTGCAAATAAAGACGGGGAAGATGTAAAAAGATGCCTGAA  
CATTCAACATTAATGAAAGATTTTCAAGAAGAAATATGTATACTAACTGCAG  
CCTTATCAAGTATATGGAAAAACACAAAGTTAAACCAGATAGTAAAGCAT  
TCCACTTGCTTCAGAAGTTTCTTACTATGGACCCAATAAAGTGAATTACC  
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TTTCAACAGTTGTCAAATCCCTACCCAAAATGAGAATTTTAAACAGAAG  
AAGAACCCTGATGACAAAGGAGCCAAAAAGAACCACCACCGGCAGCAGGGC  
CATAACCACACGAATGGAACCTGGCCACCCAGGAATCAAGACAACGGTCAC  
ACACAGGACCCCGCTTGAAGAAAGTGAGGCTTGTCTCTTACCCTAC  
CTCAGGTGGACTTTTACGGCCTCAGACTATCCGCGTTCCAATCCACATG  
CTGCCTATATCCCAACCCTGGACCAAGCACATCCCAGCCGAAGAGCAGTG  
TAGGATACTCAGCTACCTCCAGCAGGCTCCACAGGACCCACGTGAGACA  
CACGGGTACTGAGCTGCATCGGAATCTTGTCCGTGCACTGTTGTGAATGC  
TGCAGGGCTGACTGTGCAGCTCTCCGTGGGAACCTGGTATGGGCCATGAG  
AATGTACTGTACAACACACCTGCCAGTAGCCAAGTTCCTTCCACCGCT  
TTTACAGATCGGGGTAGTGGCTTCCAGTTGTACCTATTTTGGAGTTAG  
ACCTGAAAAGAAAGCGCTAGCACAGTTTGTGTTGTGGATTTGCTACTTTC  
ATAGTTAACTTGACCTGGCTCAGACTGACCAGTACTTTTTTTTCCGTGAC  
AGTCTATAGCAGTTGAAGCTGAGAATGTGCTAGGGGCAAGCGTTTGTCTT  
CATATGTCATGAATTCCTCCAGTGTAAACAACATTATCTGACCAATAGTAC  
ACACACAGACACAAGGTTTAACTGGTACTTGAAAACATACAGTAGGTGTT  
AACTCAGTGAATAAACCAGGACTCAAAGTAAGATTATTTTGGTACACCTT  
TCTTTAGTGTCTTATCAGTGAGTTGATTCAATTTCTACATTAATCAGT  
GTTTTCTGACCAAGAATATTGCTTGGATTTTTCTGAAAGTACAAAAAGCC  
ACATAGTTTTTTTCAAAAAGGTTTCAAACTCCTAAAGATTAATTTCCAA  
GTATAAGTTTGTTTTATTTTCAATCTATGACTTGACTGGTATTAAAGCT  
GCTATTTGATAGTAATTAGATATATTCTCATTGATATAAACCTGTTTGGT  
TCAGCAAACTAAATGATTGTACAGACAATGCTTTATTTTCTG  
TTGGTGTGCTTGTGGGAAAAAGAAAGAGAGATCAGATTGTTACTGTGTC  
TGTGTAGAAAAGAGTAGACATAGGAGACTCCATTTGTTCTGTACTAAGA  
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CCCTGTGCTCTCTGAAACATGTGCTGTGTCCACTCAGGGTTAAATGGATT  
AAGGGCGGTGCAAGATGTGCTTTGTTAAACAGATGCTTGAAGGCAGCATG  
CTCGTAAGAGTCATCACCCTCCCTAATCTCAAGTACCCAGGGACACAAA  
CACTGCTGAAGGCCCGCAGGGACCTCTGCCTAGGAAAGCCAGGTATTGTCC  
AAGGTTCTCCCATGTGATAGTCTGAAATATGGCCTCGTGGGAGGGGAA  
AGACCTGACCGTCCCCCAGCCGACACCCGTAAAGGGTCTGTGCTGAGGA  
GGATTAGTATACGAGGAAGGAACGCCTCTTTGCAGTTGAGACAAGAGGAA  
GGCATCTGTCTTCTGCCCCCTGCGGCAATGGAATGTCTCGGTATAAAA  
CCCGATTTTATGTTCCATCTACTGAGATAGGGGAAAACCACTTAGGGCT  
GGAGGTGGGACATGCGGCAGCAATACTGCTCTTTAAGACATTGAGATGTT  
TATGTGTATGCATATCTAAAGCACAGCACTTAATCTTTACCTGTCTAT  
GTTGCAGAGACCTTTGTTTACGTGTTTATCTGCTGACCTTCTCTCCACTA  
TTATCCTATGACCCTGCCACATCCCCCTCTCCGAGAAAACACCAAGAATG  
ATCAATAAATACTAAGGGAACCTCAGAGGCCGGCGGGATCCTCCATATACT  
GAACGCTTGTCCCTGGGCCCCCTTATTTCTTCTCTATACTTGGTCTCT  
GTGTCTTTTTCTTTTCCAAGTCTCTCGTTCCACCTAATGAGAAACACCCA  
CAGGTGTAAAGGGGCAACCCACCCCTTCATTGCTGATTTGTGAGCGTGCT  
TTAAGGTGAAAAAGCATGAATGTAACTTCTTAAAAAGGTACAGCATC  
CAATTCAAATATTTTGTCTGATTTTAAATGCTAGTTGATGTAGTGCTAT  
TAAAATTTTGTTCACATGGACACAGAGAGGGGAACAACACATACCAGGG  
CCTGTTGCGGGGTGGGGATGAGGGGAGGGAACTTAGAGGACAGGTGAACA  
GGTGCAGCAGATCACCATGGCCACATATACCTATTTAACAACCTGCAC

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GTTCTGCACACGTATCCCATTTCTTTTTTTTTTAAGAAATAGAAAAAA  
AATAAAATTTTGTTCACCTGATTCTTCCATTTTAAACTTGTTTGCATGTG  
GTTTAGGATGCCCTTACTTCAGCAAAGGAGAAGGAATAGGAGGGCCTTAG  
AATTTTTGAGGGAAAAAAACCCTATAACATACATTGTACTGTATCAAAC  
ATTTTACATGAATGACACAAGTATTCTGAATAAAAAAATAATTGAACATT  
GTTAAGAACAAGGTGTCATGTAATTTATTTTTCATAAATAAAAAATTAT  
AGTGGCTTAGACTGAAAGGAACAGAGAATTTAAAAAATTAAAAAGAAGCC  
TTAGTATATTTTGTATATAGTTTCCATGTGCCATATTTGCCATAATTGG  
ATGAGAATTTTGTGACCTCTGGCAGGGTGACCCTATATTTTCANTNTATA  
AAGCGTGCATCATACC

MVLKCHPTGDSQCAIGVRVTALGHATQTVSSIXQIIPQI.WECIRKTEAWIHPIHLLNIISI.QPGICPCSI.SNKCI.SSI.QRSASA/  
 EKGSPII.GVSKDEFCL.YCDKDKQQSIIPI.QI.KEKI.MKI.AAQKESARRPIFYRAQVGSWNMI.ESAAIHGWIFCTSCNCH  
 I:FPVGIXNXVIDFI.I.GKAQKRGTTUSE

FIG. 5

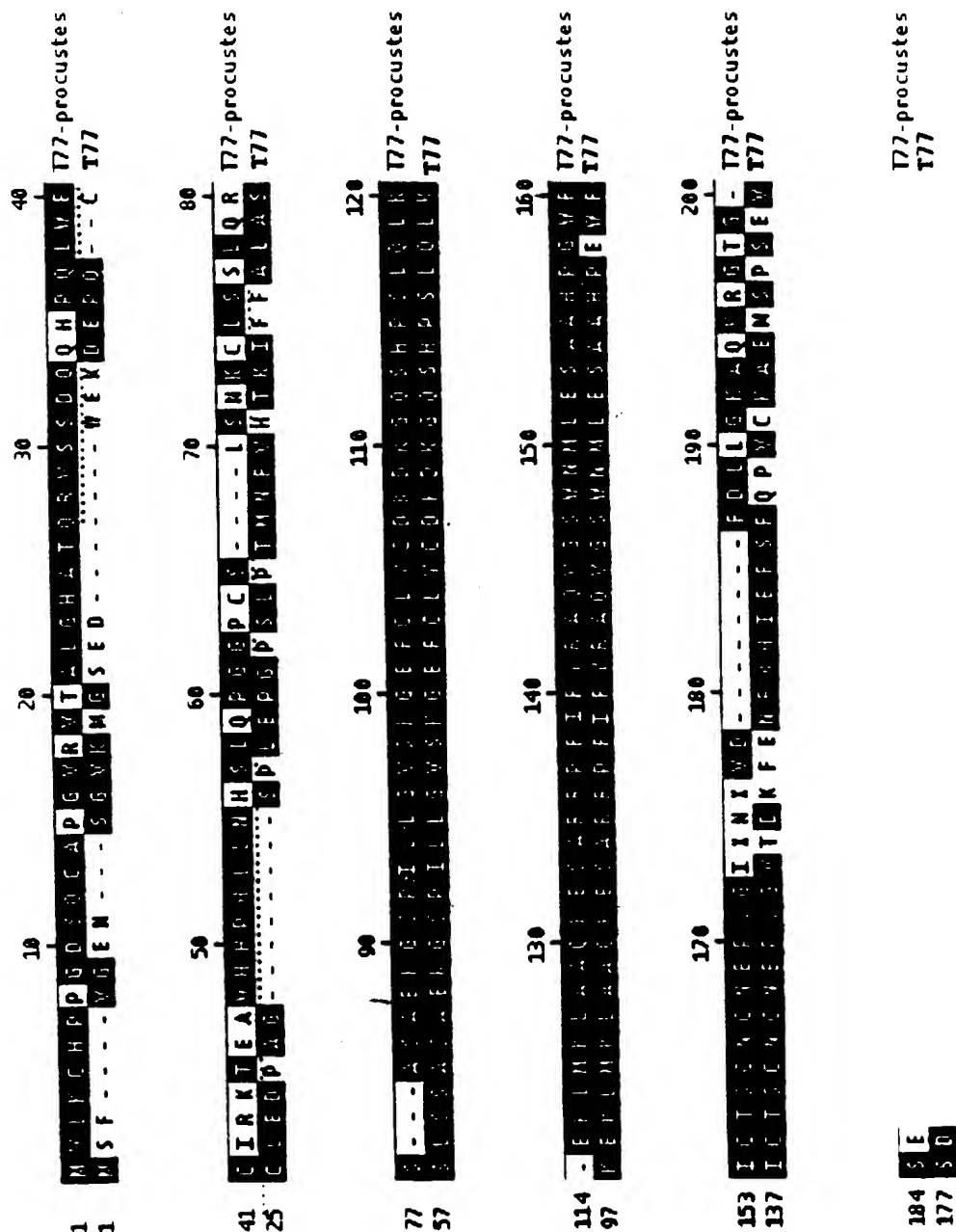


FIG. 6

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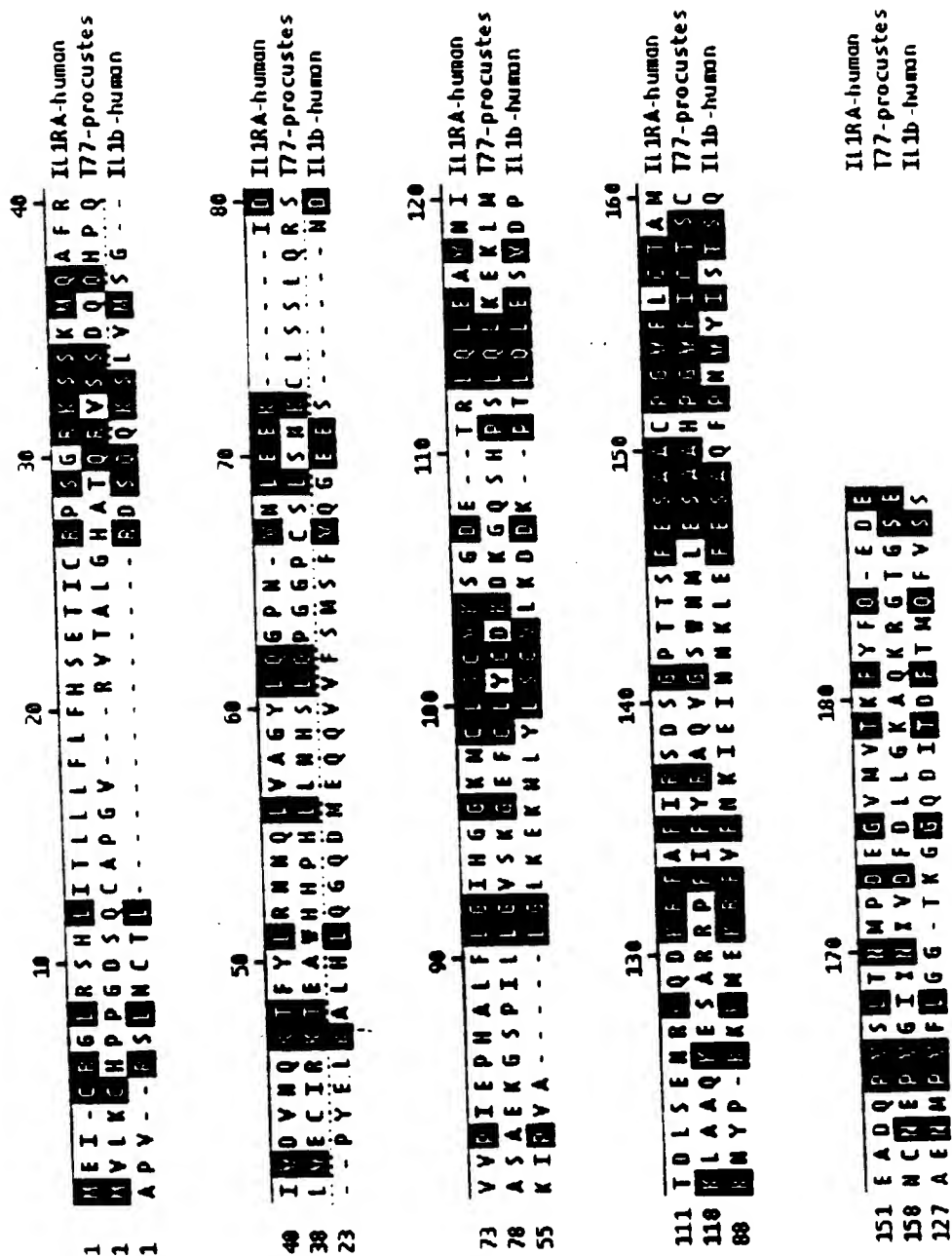


FIG. 7

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US98/16102

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : C07H 21/02, 21/04, 1/00, 14/00, 17/00; C12Q 1/68; G01N 33/53  
US CL : 536/23.1; 530/350, 387.1; 435/6, 7.1

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/23.1; 530/350, 387.1; 435/6, 7.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
DIALOG: MEDLINE, USPATFUL, WPI, BIOSIS. Search terms include author, "TANGO" and protein

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Database Medline on Dialog, US National Library of Medicine, (Bethesda, MD, USA) AN 09370320. SONNENFELD et al. 'The Drosophila tango gene encodes a bHLH-PAS protein that is orthologous to mammalian Arnt and controls CNS midline and tracheal development'. Development. November 1997, volume 124, number 22, pages 4571-82, Abstract.	1-22

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* "A" Special categories of cited documents: document defining the general state of the art which is not considered to be of particular relevance	*T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"B" earlier document published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"A" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

21 OCTOBER 1998

Date of mailing of the international search report

30 OCT 1998

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